

10-1-2002

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Christopher D. Hazuka, *Supporting the Work of Lesser Geniuses: An Argument for Removing Obstructions to Human Embryonic Stem Cell Research*, 57 U. Miami L. Rev. 157 (2002)

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Supporting the Work of Lesser Geniuses: An Argument for Removing Obstructions to Human Embryonic Stem Cell Research

BY
CHRISTOPHER D. HAZUKA*

INTRODUCTION

There is “no realm of medicine that might not be touched” by embryonic stem (ES) cell research, according to Nobel laureate and former National Institutes of Health (NIH) director, Harold Varmus.¹ Not only will ES cell-based therapies help save lives, but the development of ES cell-based treatments will promote the growth of the biopharmaceutical industry, in addition to contributing to the economy at large.² In order to recognize the benefits of ES cell research, scientists require financial support from public sources, private sources, or both. Two independent roadblocks have recently threatened financial support for ES cell research: the presence of broad patent claims covering the subject matter and moral concerns regarding the research.

Research on ES cells is just beginning. Therapeutic applications as well as basic research results await discovery.³ But patents⁴ granting broad property rights covering the human ES (hES) cell to the Wisconsin Alumni Research Foundation⁵ (WARF) will limit exploration of the

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1. John Davidson, *Australia's Gene Genies*, AUSTRALIAN FIN. REV., Sep. 15, 2001, at 41, available at 2001 WL 27344355. See generally *Stem Cell Research News* (2001), at <http://www.stemcellresearchnews.com>.

2. The “market for stem cell-based treatments could be worth \$US 200 billion a year or more.” Davidson, *supra* note 1, at 41.

3. “Whatever form stem cell therapy takes, whether it’s cloned from the patient, tissue-matched from a donor or stimulated endogenously, one thing is certain: most of the key discoveries are yet to be made, and most of the intellectual property is yet to be staked out.” *Id.* See also Center for Science, Technology, & Congress at the American Association for the Advancement of Science, *From the Hill: New Limits on Funding of Stem Cell Research Questioned*, ISSUES SCI. & TECH. 29 (2001).

4. U.S. Patent No. 5,843,780 (issued Dec. 1, 1998); U.S. Patent No. 6,200,806 (issued Mar. 13, 2001).

5. WARF is the organization that handles the patenting of inventions emanating from the University of Wisconsin. This patent holder is Dr. James Thomson, a professor at the University of Wisconsin.

properties and potential uses of hES cells.⁶ WARF now owns property rights covering the hES cell—a product of nature, whose existence was already known. WARF's inventive leap was not the discovery of the hES cell but rather the method for maintaining hES cells in an artificial environment (in “culture”) in such a way that they retain the ability to transform into different cell-types, and the production of some unique hES cell-lines.⁷ The contribution described in the WARF patents is important because it enables scientists to use these cells to make mature cells, organs, and tissues that can be used therapeutically. Nevertheless, now that WARF owns broad property rights to any hES cell—rights that are not coextensive with the inventive contribution to society—any researcher must negotiate with WARF before using hES cells, even if that researcher isolates new hES cells or uses a new method to do so.⁸ The hES cell patent product claims serve as an example of the phenomenon whereby downstream improvement-type research is stifled when patents containing broad claims to basic research discoveries are issued.⁹

This article will analyze whether the incentive goals of the patent laws are properly served when such broad claims to upstream or pioneering inventions¹⁰ are granted. In effect, it uses the hES cell claims as a case study. Although it is true that patents provide incentives for inventors to invest resources in creating a specific invention, the patent system may overlook the implications of such property rights on the incentives of the community of inventors as a whole. The effects of granting a limited monopoly right to a single entity must be weighed against the negative effects that such a monopoly will have on subse-

6. Sheryl Gay Stolberg, *Stem Cell Research Is Slowed by Restrictions, Scientists Say*, N.Y. TIMES, Sept. 25, 2002, at <http://www.nytimes.com/2002/09/26/politics/26stem.html>; *Bush Stem Cell Policy Has Not Met Promise*, ASCB NEWSL., Sept. 2002, at 11; *Researchers Dub President's Stem Cell Policy a Failure*, ASCB NEWSL., Nov. 2002, at 13; G. Steven McMillan et al., *An Analysis of the Critical Role of Public Science in Innovation: The Case of Biotechnology*, 29 RES. POL'Y 1, 1 (2000) (discussing the importance of federal funding of basic research for biotechnology companies, in contrast to pharmaceutical companies).

7. See discussion *infra* Part I.A.

8. See discussion *infra* Part I.D.

9. See discussion *infra* Part II.A. (defining downstream, basic and applied research, and improvement inventions).

10. See discussion *infra* Part II.A. (defining upstream and pioneering inventions).

quent innovators¹¹: the so-called lesser geniuses.¹²

Part of the problem results from the fact that the U.S. Patent and Trademark Office (PTO) properly does not consider the broad effects of the issuance of a patent on the industry, academy, economy, or society. Instead it looks only to its mandate to award property rights to inventors who seemingly pass the bars set by patent doctrines. While the PTO is correct in not attempting to take into account the broader implications of issuing a patent, it must make sure that the traditional bars to patentability are sufficiently strictly enforced. The patent system can then achieve its goal of providing incentives to all parties—the pioneer inventors and the lesser geniuses—who may be involved in the development of an invention. The hES cell patents provide a real-world context in which to address this issue. Within this debate lie questions of where and when property rights should be granted and protected. For example, should the patent system promote the development of research tools or products, and purification or isolation of products of nature? And how should the patent system balance incentivizing upstream pioneering discoveries and downstream improvement-type inventions?

The problem of the WARF patents impeding hES cell research is exacerbated by a recent decision made by President George W. Bush to fund with federal money only research on a limited number of hES cell-lines.¹³ President Bush was troubled by hES cell research because of ethical concerns: to obtain an hES cell a living human embryo must be destroyed.¹⁴ To some, that is tantamount to murder.¹⁵ On August 9, 2001, President Bush attempted to find a compromise position: he decided to limit federal funding to research on hES cells that existed

11. In economic terms, the general question is whether “assuming the patent system . . . stimulat[es] technological innovation, [are] the social and economic costs of distortion in the allocation of resources and the monopoly rents exacted by patent holders during the lives of their patents greater than the social benefits of the new technologies?” David Silverstein, *Patents, Science, & Innovation: Historical Linkages & Implications for Global Technological Competitiveness*, 17 RUTGERS COMPUTER & TECH. L.J. 261, 303 (1991). Brian Peckham, *Should the U.S. Patent Laws Be Abolished?*, 11 J. CONTEMP. L. 389 (1985). “It is obvious that the legitimate interests of companies may not coincide with scientists’ research plans or our nation’s public health policy.” Anthony Shadid, *Kennedy Set to Speak Out Against Stem Cell Limits*, BOSTON GLOBE, Sep. 5, 2001, at A1 (quoting Professor Douglas Melton’s prepared comments before the Senate Health, Education, Labor, and Pensions Committee).

12. Judge Jerome Frank used the expression “lesser geniuses” in *Katz v. Horni Signal Mfg. Corp.*, 145 F.2d 961, 961 (2d Cir. 1944).

13. See *infra* text accompanying note 34.

14. See *infra* text accompanying note 21.

15. See Laurie Goodstein, *Abortion Foes Split over Bush’s Plan on Stem Cells*, N.Y. TIMES, Aug. 12, 2001, at <http://www.nytimes.com/2001/08/12/politics/12RIGH.html>; see also Randall Terry, on NewsHour with Jim Lehrer (PBS television broadcast, Aug. 9, 2001), available at http://www.pbs.org/newshour/bb/health/july-dec01/stemcells_8-9.html.

before his speech.¹⁶ Federal funding is not permissible for hES cells obtained by destroying a human embryo after August 9, 2001.¹⁷

The hES cell patents along with President Bush's decision provide an opportunity to ask how federal funding interacts with the incentive goals of the patent system with respect to upstream, basic research. The two systems interact in various ways. First, federal funding and the patent system can be seen as complementary. Second, federal funding may provide a mechanism through which to constrain broad property rights. Although it is always important to ensure that patent property rights are appropriately issued, it is crucial in the absence of federal funding. This article will assume that federal funding does not exist for future hES cell research. It will focus on the implications of the WARF product patent claims on future incentives of private firms to fund or conduct hES cell research.

Regarding the first type of interaction, the hES cell subject is particularly illustrative because it is at the nexus of the incentive problem: the patent system (and private investment) is meant to pick up where federal funding leaves off. Without federal funding, private organizations must have incentives to support research because scientists must turn to private sources for money. These sources generally want something in return: in some transactions, property rights to the discoveries or inventions. Indeed, the scientist who purified hES cells is a federally funded university researcher who is primarily interested in basic biomedical research.¹⁸ Nevertheless, he was forced to partially turn to private funding from the biotechnology company, Geron, to carry out his hES cell work because of the government's refusal to fund hES cell research.¹⁹ As a result, he assigned some of the property rights to hES cells to Geron.²⁰ But this system only works when property rights do not impede privately funded scientists from conducting research, and when there are property rights to offer to the source of the funds. Based

16. See *infra* text accompanying note 34.

17. Katharine Q. Seelye, *Bush Gives His Backing for Limited Research on Existing Stem Cells*, N.Y. TIMES, Aug. 10, 2001, at 2001 WL 26414517. See <http://escr.nih.gov/> for a list of the hES cells-lines on which research using federal funding can be performed. The moral questions surrounding hES cell research are difficult and several articles have been written analyzing them. See, e.g., Jason H. Cassell, *Lengthening the Stem: Allowing Federally Funded Researchers to Derive Human Pluripotent Stem Cells from Embryos*, 34 U. MICH. J.L. REFORM 547 (2001); Nelle S. Paegel, *Use of Stem Cells in Biotechnological Research*, 22 WHITTIER L. REV. 1183 (2001). While this article will not look at those issues, for the purposes of this article, I will consider hES cell research moral because of the broad and important benefits it may offer sick, diseased, and suffering people. *Stem Cells: Potential for Good?*, ECONOMIST, Aug. 18, 2001, at 59. The research should be stimulated at the very least by the incentives provided by the patent system.

18. Frederic Golden, *Cellular Biology: Stem Winder*, TIME, at 27 (Aug. 20, 2001).

19. *Id.*

20. *Id.*

on this rationale, this article argues that overly broad patent rights to upstream products of nature should not be granted because they unnecessarily remove incentives to future private organizations that wish to fund or conduct downstream research. The presence of such broad patent claims will reduce the value of any future work, which may infringe it. Thus, private funding will not complement federal funding.

Regarding the second interaction, federal funding of scientists promotes further development of discoveries, thus increasing the chances that patent claims can be narrowed or “invented around” by future work. In other words, in the absence of federal funding, the property rights held by private organizations will generally be larger, stronger, and thus more preclusive of the ability of other scientists to perform research in the same field. It is even more important in the absence of federal funding to ensure that the patent claims do not cede more territory to the patent holder than is warranted by the patent disclosure’s contribution to society. These ideas will be developed further in Parts II and III.

Part I describes the science underlying ES cell research and its important applications. It then summarizes the legal and political environment surrounding the use of the technology, including decisions regarding federal funding of the research. Finally, it turns to the issued patents that cover ES cells. Part II discusses the theoretical implications of broad patent claims on subsequent development of technology in general and as applied to hES cell research.

Part III describes how the patent system can better stimulate hES cell research and therapy development, as well as general biotechnology research, by insisting on a stricter application of patentability requirements. Application of higher bars to patentability can be achieved by enforcing the existing patent statutes and case law. In particular, the PTO and the courts should require that the invention be new, useful, and have a component of human intervention, in other words, be an “invention.” Specifically, Part III argues that a court should invalidate the hES cell patent product claims on traditional patentability grounds, including the utility, written description, enablement, and novelty requirements. Alternatively, but less desirably, the scope of the hES cell product claims could be interpreted narrowly. The scope of the claims should accurately reflect the disclosed invention.

Briefly, this analysis as applied to the hES cell patents results in the conclusion that the broad WARF patents product claims are invalid for the following reasons. First, the material they cover is not new; hES cells already existed in nature. Second, the biological matter as claimed was not changed in any way by humans. Third, no clear use, other than research use, has yet been demonstrated. Fourth, the inventive leap or

contribution to society was not the discovery or purification of hES cells, but: (1) discovery of a way to keep them alive in an artificial environment in such a way that they can develop into many mature cells; and (2) the production of a handful of unique hES cell-lines. As the method is the inventive contribution to society, this method, and not all freshly purified hES cells, should be protected by a property right. Similarly, just as a handful of human-made cell-lines were invented and contributed to society, WARF should receive patent product claims to cover only those specific cell-lines. However, as WARF did not invent *the* hES cell, the claims to all freshly purified hES cells should be invalidated by the courts. This analysis suggests that similar attempts to claim property rights on fresh purifications of biological matter should be closely scrutinized by the PTO and the courts.

Part IV inquires into the wisdom of Congress or the courts declaring, as a quick fix, certain areas of science patentable. The issue is dissected into two distinct subjects. First, Congress could, in general, declare broad areas of technology off-limits to patenting. For example, freshly purified human cells, human cells in general, or even broader categories of biotechnology inventions could be declared unpatentable. Second, either Congress or the courts could remove the property rights solely with respect to hES cells. For example, Congress could address the issue of the hES cell patents as part of its deliberation over how to respond to President Bush's hES cell funding decision. Part IV concludes that neither of these options is desirable. In general, Congress and the courts should avoid declaring certain areas of biotechnology unpatentable. It is difficult to separate out inventive fields for such purposes, especially in unpredictable technologies. By enforcing existing patent law instead, the system's flexibility will be maintained. The patent system relies on certainty, as industry players need to know how to value patent rights. Congress should avoid intervening in the hES patent situation. Although voiding patent claims as a part of policy-making would be a quick remedy to the problems raised by the WARF patents, Congress would needlessly introduce uncertainty into the system.

I. THE PRESENT STATE OF hES CELL RESEARCH

This Part presents an overview of the present science understanding of hES cells and the inventive leap that led to their successful purification and patenting. It discusses some applications of hES cell research, both as illustrations of the importance of hES cell technology in developing cures for human disease and as examples of the reach of the WARF patents. It concludes with President Bush's decision on how to

regulate hES cell research and an introduction to the WARF patents and their implications on future innovation.

A. Stem Cell Science

An hES cell²¹ can develop into many of the roughly 220 different types of cells found in a mature human being.²² Once a cell develops into a characteristic mature cell, it is then committed to that fate.²³ For example, a mature skin cell normally does not transform into a brain cell. In contrast, ES cells are unique in that they can be manipulated into differentiating into different cell types.²⁴ It is this property that makes these cells useful to scientists in their quest to develop new therapies for treating disease.

After an egg is fertilized by a sperm cell, it gives rise to every type of cell in the developing and mature human being. This fertilized egg contains exactly the same genetic sequence as most developed cells in the adult person to which it gives rise.²⁵ The fertilized egg begins to divide, producing identical ES cells, each of which is capable by itself of maturing into a person; in fact, this is the explanation for identical twins.²⁶ These cells continue to divide, forming the blastocyst, a sphere of cells that is hollow in the middle except for what is called the inner

21. See National Institutes of Health, *Stem Cells: A Primer* (2000), at <http://www.nih.gov/news/stemcell/primer.htm> [hereinafter NIH]; see also Audrey R. Chapman et al., *Stem Cell Research and Applications: Monitoring the Frontiers of Biomedical Research* (1999), at http://www.meta-library.net/stemcell/index_body.html; Rick Weiss, *A Crucial Human Cell Isolated, Multiplied: Embryonic Building Block's Therapeutic Potential Stirs Debate*, WASH. POST, Nov. 6, 1998, at A01.

22. See, e.g., Laura DeFrancesco, *Determining Embryonic Stem Cell Potential*, 16 SCIENTIST 28 (2002).

23. Of course, advances in biological science may change this fundamental property.

24. Different stem cells might vary in their ability to become different types of cells. Some are called toti potent, meaning that they are thought to be capable of becoming any type of cell. NIH, *supra* note 21. Others are called pluri potent because they are capable of developing into any cell derived from the three main germ cell layers, but are perhaps more limited in their capacity than are toti potent cells. *Id.* Finally, there are multi potent stem cells, which have fewer developmental possibilities than the prior two. *Id.* Multi potent stem cells are found in adult tissue, such as the blood or bone marrow. BRUCE ALBERTS ET AL., *MOLECULAR BIOLOGY OF THE CELL* 1283 (4th ed. 2002). ES cells derived in technically different ways might retain the ability to differentiate in distinct ways, into different cell types, and the techniques for maintaining stem cells in labs might alter their ability to differentiate. *Id.* at 474. Moreover, hES cells isolated from different humans will be genetically distinct. Thus, depending on from where and how the ES cells are isolated and maintained, they will have distinct identities and properties. This scientific fact further illustrates the problem with issuing a patent covering all hES cells.

25. An intense area of scientific inquiry for decades has been the attempt to understand why cells with the same genetic components (for example, the fertilized egg and an adult skin cell) behave so differently. ALBERTS ET AL., *supra* note 24, at 1157.

26. See NIH, *supra* note 21.

cell mass.²⁷ The inner cell mass gives rise to almost all of the tissues of a human body.²⁸

In order to isolate and culture hES cells, Dr. James Thomson of the University of Wisconsin collected human embryos in the blastocyst stage from in vitro fertilization (IVF) clinics, and removed the inner cell mass.²⁹ He was the first person to keep hES cells alive in culture in their hES cell state.³⁰ In the process, he developed five distinct hES cell-lines.³¹ Cell-lines are distinct from freshly purified cells because they may have unique properties.³² It is important to keep in mind that these two contributions represented the inventive leap that he contributed to society. He did not contribute the hES cell itself, which was certainly known prior to his invention.³³ His contribution was to keep the hES cells alive in culture for over a year in their hES cell state in such a way that they retained their ability to transform into mature cells and to develop a handful of hES cell-lines.

B. *Applications of hES Cell Research*

The excitement generated by hES cell research is justifiable. First, the importance of hES cells in scientific research cannot be overstated.³⁴ For example, scientists need such an early stage cell in order to understand how genes are turned on and off in development and in cancer.³⁵ They will also be useful for developing and testing drugs; they could dramatically speed up the drug discovery process.³⁶ For example, scientists could test potential anticancer drugs on cells or tissues derived from hES cells that were derived from a person who suffers from the cancer. Presently, scientists must use animal models and human testing in clinical trials. More exotically, scientists envision a new era of "cell therapies."³⁷ Thomas Okarma, CEO of Geron (a company specializing in stem cell technology), believes that "living cells will be tomorrow's

27. *Id.*

28. At this stage, these cells are now pluri potent because they are not capable, by themselves, of forming a human being, but are capable of collectively forming the tissues of a human being. *Id.*

29. J.A. Thomson et al., *Embryonic Stem Cell Lines Derived from Human Blastocysts*, 282 SCIENCE 1145 (1998).

30. See discussion *infra* Section II.D. (describing more of his method for succeeding in keeping the ES cells alive in culture in their pluri-potent state).

31. See Thomson et al., *supra* note 29.

32. ALBERTS ET AL., *supra* note 24; see also *infra* notes 232 and accompanying text.

33. ALBERTS ET AL., *supra* note 24, at 1308.

34. Chapman et al., *supra* note 21, at 6.

35. See NIH, *supra* note 21.

36. See *id.*

37. See *id.*; Chapman et al., *supra* note 21, at 5-6.

pharmaceuticals.”³⁸ For example, patients with Parkinson’s Disease suffer from degeneration of dopaminergic neurons in their brains.³⁹ In some diabetes patients insulin-secreting cells are impaired.⁴⁰ Some cancer patients need bone marrow transplants. Replacements for these lost cells could be derived from hES cells and then transplanted into these patients. Organs will likely be developed in vitro. Researchers have already used ES cells to produce heart cells that, as a population, beat in unison in a dish.⁴¹ In general, if one needs new cells, tissues, or organs, this technology could be the answer. Hopefully, the availability of hES cell-based therapies will eliminate both the need to ask people to donate organs and tissues, and the problem arising from the fact that there are far too few donors today.⁴²

The greatest benefits of hES cell research likely will be realized in combination with therapeutic human cloning techniques.⁴³ One particularly promising area of future research involves the use of hES cells isolated from cloned human embryos to custom make immuno-compatible replacement tissues, cells, and organs. Therapeutic human cloning may be used to produce a human embryo clone of the person in need of transplantable tissue. hES cells would be derived from this cloned embryo when it is in the blastocyst stage. In this way, all hES cells—and differentiated cells and tissues resulting from them—would be

38. Associated Press, *Seeking Profit in Stem Cells*, (Jul. 13, 2001), available at www.wired.com/news/print/0,1294,45232,00.html.

39. ERIC R. KANDEL & JAMES H. SCHWARTZ, *PRINCIPLES OF NEURAL SCIENCE* 529 (2nd ed. 1985).

40. See NIH, *supra* note 21.

41. Weiss, *supra* note 21, at A01.

42. Monique C. Gorsline & Rachelle L.K. Johnson, *The United States System of Organ Donation, the International Solution, and the Cadaveric Organ Donor Act: “And the Winner Is . . .”*, 20 J. CORP. L. 5, 6-7 (1995); Laurel R. Siegel, *Re-Engineering the Laws of Organ Transplantation*, 49 EMORY L.J. 917, 917 (2000).

43. See NIH, *supra* note 21; Anne McLaren, *Cloning: Pathways to a Pluripotent Future*, 288 SCIENCE 1775 (2000); Robert P. Lanza et al., *The Ethical Validity of Using Nuclear Transfer in Human Transplantation*, 284 J. AMER. MED. ASS’N 3175 (2000); John D. Loike, *Member Opinion: Bioethical and Legal Boundaries of Human Cloning*, ASCB NEWSL., July 2001, at 2. Indeed, many fear stem cell research precisely because of its application of human cloning techniques: “the greatest anxiety about stem-cell research is that it will make human cloning respectable. Many of the techniques being perfected for the medical application to stem cells are just a hop, skip, and a jump away from those that could apply to reproductive cloning.” Gregg Easterbrook, *Cloning and a Change in the Meaning of Life: Stem-Cell Research*, 413 CURRENT 19 (1999). Indeed, President Bush did not even attempt to compromise on the cloning issue. While nearly everyone agrees that cloning to produce adult human clones (“reproductive cloning”) should be banned, many scientists, ethicists, and politicians believe that the technology should remain open for use as a research tool or to prepare hES cells (“therapeutic cloning”). Nevertheless, President Bush has called for a ban on all aspects of the technology. See Sonya Ross, *President Bush Presses for Ban on Human Cloning*, CHARLESTON GAZETTE, Apr. 11, 2002, at 1A, available at 2002 WL 5192113.

genetically identical to the person who needs the replacement tissue. Such genetically identical tissues are desirable because it is believed that they may eliminate many of the problems associated with immuno-rejection of transplanted tissue.⁴⁴

In the future, organs and transplantable cells and tissues may be immuno-compatible and in ready supply. Asking relatives to donate organs, using organs from deceased people or from animals, using mechanical organs, and requiring blood and tissue banks might become obsolete. This great advantage of hES cell research may not be realized using adult stem cells. The attempt to create a genetically identical cell or tissue will likely require the creation and destruction of a human blastocyst.

C. *Political and Legal Reaction to Stem Cell Science: President Bush's Decision Allowing Federal Funding of hES Cell Research*

President Bush's response to hES cell research was influenced by prior regulation of embryo research, beginning with IVF technology.⁴⁵

44. NIH, *supra* note 21.

45. Legislation and administrative decisions concerning IVF through 2001. In 1974, Congress established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, in part to assess the desirability of research on the human fetus. REPORT & RECOMMENDATIONS OF THE NBAC, ETHICAL ISSUES IN HUMAN STEM CELL RESEARCH 29 (1999) [hereinafter NBAC REPORT]. This Commission's recommendations resulted in *Protection of Human Subjects*, 45 C.F.R. § 46, Part 46, which contains regulations on IVF promulgated by what is now the Department of Health and Human Services (DHHS). These regulations, which are utilized by most agencies or departments that administer federal funds for human research, cover all "grants and contracts [administered by the DHHS] supporting research, development, and related activities" involving IVF. 45 C.F.R. § 46.201 (1994). To achieve funding from the DHHS, all applications or proposals involving human IVF must be reviewed by an Ethical Advisory Board (EAB). See 45 C.F.R. § 46.204(d), nullified by § 121(c) of the NIH Revitalization Act of 1993, Pub. L. 103-43, 107 Stat. 122, § 121(c) (1993); see also 59 Fed. Reg. 28,276 (June 1, 1994).

Initially, an EAB recommended funding for embryo research. NATIONAL INSTITUTES OF HEALTH, DEVELOPMENT OF NIH GUIDELINES GOVERNING RESEARCH INVOLVING HUMAN IN VITRO FERTILIZATION AND THE PREIMPLANTATION EMBRYO (1995). No IVF research was funded with federal money, however, because the NIH never initiated any projects. NBAC REPORT, *supra* at 42. This Board reviewed one application for IVF research, but its recommendations were not followed, and the Board was disbanded until the NIH Revitalization Act of 1993. *Id.* Interestingly, in its one review, the EAB approved federal funding of IVF research pursuant to the following guidelines: (1) informed consent from donors of the gametes; (2) the scientific goal of the research was not reasonably attainable by other means; and (3) the embryo must not be maintained in vitro beyond the stage normally associated with the completion of implantation (normally about fourteen days post fertilization). *Id.* No subsequent EAB was impaneled and, accordingly, no embryo research was funded. This de facto moratorium on human fetal, IVF, and embryonic research was lifted in 1993 with the passage of the NIH Revitalization Act. National Institutes of Health Revitalization Act of 1993, *supra*. Not only was the EAB impaneled, but the presumption was reversed: research could now be funded unless the EAB recommended

This background informed the debate over whether to regulate research involving hES cells.⁴⁶ Major ethical concerns are raised when considering whether to fund (or even allow) this type of research. On one hand, many are concerned with destroying a human embryo, viewing the embryo as a living person.⁴⁷ Others are simply afraid of “playing God” with biology.⁴⁸ On the other hand, such research may help save lives,

otherwise. NBAC REPORT, *supra*, at 42. But because of the subject’s sensitivity NIH Director Harold Varmus established a Human Embryo Research Panel to attempt to devise standards for determining which research could be funded consistent with ethical considerations. 59 Fed. Reg. 28,874, 28,875 (June 3, 1994) (notice of meeting). Similar to the conclusions of the EAB almost fifteen years before, this new Panel considered ethically permissible the use of IVF for certain research purposes. National Institutes of Health, *Report of the Human Embryo Research Panel*, Sept. 27, 1994 [hereinafter NIH, REPORT]; Laurie McGinley, *U.S. Panel Backs Human-Embryo Studies*, ASIAN WALL ST. J., Sept. 29, 1994, at 26. Nevertheless, both President Clinton and Congress clarified that federal funds could not be used for experiments in which embryos are destroyed. Press Release, Office of the White House Press Secretary, Statement by the President (Dec. 2, 1994); Balanced Budget Downpayment Act of 1996, Pub. L. No. 104-99, § 128, 110 Stat. 26, 34 (1996). As a result, Dr. Thomson first isolated hES cells by working “in a room in which not a single piece of equipment, not even an electrical extension cord, had been bought with federal funds.” Weiss, *supra* note 21.

46. Legislation and administrative decisions focused on hES cell research through 2001. The Human Embryo Research Panel, *supra* note 45, found it permissible to create embryos using IVF techniques for the sole purpose of purifying stem cells. NIH, REPORT, *supra* note 45. Yet President Clinton issued a directive order specifying that such research was impermissible. Press Release, Office of the White House Press Secretary, Statement by the President (Dec. 2, 1994). Moreover, Congress, in what is known as the “Dickey Amendment” to a 1995 appropriations bill, further narrowed the research subject to federal funding, excluding funding for: (1) the creation of a human embryo or embryos for research purposes; or (2) research in which a human embryo or embryos are destroyed, discarded, or knowingly subjected to risk of injury or death greater than that allowed for research on fetuses in utero under 45 C.F.R. § 46.208(a)(2) and § 498(b) of the Public Health Service Act (42 U.S.C. § 289g(b)). Pub. L. No. 104-99, 110 Stat. 26, 34 (1996). Omnibus Consolidated and Emergency Supplemental Appropriations Act for Fiscal Year 1999, Pub. L. No. 105-277, 112 Stat. 2681-386 (1998). The definition of human embryo for the purposes of this legislation is “any organism, not protected as a human subject under 45 CFR § 46 as of the date of the enactment of this Act, that is derived by fertilization, parthenogenesis, cloning, or any other means from one or more human gametes or human diploid cells.” Pub. L. No. 104-99, 110 Stat. 26, 34 (1996).

Harriet Rabb, general counsel of the DHHS, wrote a memorandum explicating a loophole through which funding of hES cell research could escape. *Memorandum from Harriet Rabb, to Harold Varmus* (Jan. 15, 1999). The reasoning was that hES cells are not human embryos. Thus, federal money could be applied to hES cell research as long as that money was not used to isolate the hES cells (a process that results in the destruction of the embryo); federally funded researchers could thus simply rely on private funding to isolate the hES cells. On August 25, 2000, federal money for hES cell research was finally authorized on the conditions that the hES cells were obtained without federal funds “from embryos that were created for the purposes of fertility treatment and were in excess of the clinical need of the individuals seeking such treatment.” *NIH Guidelines for Research Using Human Pluripotent Stem Cells*, at www.nih.gov/news/stemcell/stemcellguidelines.htm.

47. See *supra* note 15 and accompanying text.

48. See, e.g., Ronald Bailey, *Remaking Eden: Cloning & Beyond in a Brave New World*, 30 REASON 63 (1998) (discussing the moral implications of human cloning and, by extension, hES cell research).

cure disease, and eliminate painful or debilitating disorders. Against this background, on August 9, 2001, President Bush announced a compromise position, allowing federal funding for experiments using hES cells obtained before his speech, but not for those using cells obtained afterward.⁴⁹ This decision was meant to satisfy those who lobbied for the research and those who feel that destruction of a human embryo is morally repugnant.

The reaction was mixed. For example, the conservative Christian group, Focus on the Family, was “pleasantly surprised” with the decision, while the National Conference of Catholic Bishops found it “morally unacceptable.”⁵⁰ And while scientists breathed a sigh of relief that the research was not banned altogether, immediate concerns arose regarding the number and viability of the cell-lines that existed prior to President Bush’s speech.⁵¹ Specifically, it is likely true that: (1) the existing cell-lines only represent a very narrow range of the genetic diversity present in the human species; (2) cells, tissues, and organs made from the existing cell-lines may not be safe for therapeutic use in humans;⁵² (3) the existing cell-lines are not robust enough to last long enough for many laboratories to use them over an extended period of time; and (4) it may be difficult for scientists to obtain the existing cell-lines at a reasonable cost and time.⁵³

The first concern alone is troubling. hES cells isolated from different humans will be genetically distinct. Thus, depending on from where and how the ES cells are isolated and maintained, they will have distinct

49. See Seelye, *supra* note 17 and accompanying text.

50. Goodstein, *supra* note 15.

51. “In practice, however, . . . there are far fewer than 60 useful lines available to researchers. Some existing lines are hard to grow; some are ill-characterised; some are tied up in patent paperwork that limits their use.” *Stem Cells: Potential for Good?*, *supra* note 17. See also *supra* note 6; NIH Human Embryonic Stem Cell Registry, U.S. Dept. of Health & Human Servs. web site, at <http://escr.nih.gov>; Adam Clymer, *The Stem Cell Battle Moves to Congress*, N.Y. TIMES, Aug. 12, 2001, available at www.nytimes.com/2001/08/12/politics/12CONG.html; Krista Conger, *Researchers Have Mixed Reactions to President’s Stem Cell Decision*, STAN. REP., Aug. 22, 2001, available at <http://news-service.stanford.edu/news/august22/stemcellddecision.html>; Will Dunham, *Most Cell Colonies Not Yet Usable—U.S. Official*, REUTERS (2001), available at http://dailynews.yahoo.com/hx/nm/20010905/pl/health_stemcell_dc_5.html. In addition, the most prestigious body of scientists in the United States, the National Academy of Sciences, called for the production of more stem cell lines. Sheryl Gay Stolberg, *Controversy over Cloning Reignites in Congress*, N.Y. TIMES, Dec. 18, 2001, available at <http://www.nytimes.com/2001/12/18/health/genetics/18CELL.html>. This report, issued on Sep. 11, 2001, was disregarded by the media in light of the terrorist attacks.

52. For example, some scientists are concerned that these cell-lines are prepared and maintained in cultures with mouse cells. See Center for Science, Technology, & Congress at the American Association for the Advancement of Science, *supra* note 3, at 30.

53. See *id.*

identities and properties.⁵⁴ This is critically important for research and therapeutic purposes. From a research perspective, if a scientist is interested in finding therapies for a specific disease, it would be valuable to obtain hES cells derived from a person who is known to suffer from that disease.⁵⁵ The scientist may then study how hES cells with the same putative disease-inducing genes mature into diseased cells, tissues, or organs. From a therapeutic perspective, the first, second, and third concerns are critical; medical researchers need to ensure that hES cells are prepared so that they are safe for introduction into people.⁵⁶ Learning how to prepare hES cells safely requires experimentation. The existing hES cell-lines already may be inappropriate for human use. Moreover, different laboratory methods might have important implications for the usefulness of an hES cell-line. For example, hES cells derived in technically different ways might retain the ability to differentiate in distinct ways, into different cell types. Similarly, the techniques for maintaining hES cells in laboratories might alter their ability to differentiate.

More generally speaking, according to James Thomson, "The current ban in the United States on the use of federal funding for human-embryo research discourages the majority of the best United States researchers from advancing this promising area of medical research."⁵⁷ Lack of funding from the federal government puts the burden of supporting hES cell research on the private sector, but companies are not picking up the slack. For example, as of 2002, Geron provided more money in support of hES cell research to academic institutions than any other company.⁵⁸ That amount was only about \$4.7 million in 2001 and about \$3.4 million in 2002.⁵⁹ By contrast, the NIH last year contributed over thirty-one times that amount to human *adult* stem cell researchers.⁶⁰ An additional problem is that, in contrast to federally funded researchers, private companies need not disclose their results or their research.

54. ALBERTS ET AL., *supra* note 24.

55. Ruthann Richter, *Stem Cell Pursuits*, 19 STAN. MED. 11 (2002).

[Y]ou want to be able to obtain samples from people with a known genetic predilection for a disease, so that, [for example,] when you develop a blood vessel cell from an [ES] cell, it comes from someone with a family with a high risk of heart disease and stroke. That way you would be working on something really relevant to that disease.

Id. (quoting Dr. Irving Weissman).

56. Conger, *supra* note 51 (quoting Dr. Irving Weissman).

57. Wired News Report, *Human Cell Growth Patented*, WIRE, Dec. 9, 1998, at www.wired.com/news/print/0,1294,16730,00.html.

58. The "next biggest contributor to stem cell research, the Juvenile Diabetes Research Foundation, spent only \$1.2 million last year." Paul Elias, *Company Bets on Embryonic Research*, POPSCI WIRE, Aug. 2, 2001 (on file with author).

59. *Id.*

60. *Id.*

Thus, what little hES cell research is occurring is being performed without oversight.⁶¹

As time has passed, proponents of both sides have voiced disappointment in President Bush's decision.⁶² Congress's response to the decision has been mixed. For example, Republican Senator Arlen Specter has introduced a bill that would allow federally funded scientists not only to use any hES cell-line in experiments, but to create new hES cell-lines by extracting them from embryos.⁶³ Disregarding a veto threat by President Bush, members of the House and Senate called for hearings to determine whether funding should be extended to the production of new hES cell-lines.⁶⁴ Nevertheless, President Bush's decision stands for now; the result is that most hES cell research will likely be funded by private organizations.

D. Patent Issues Relating to hES Cell Research

To understand its effects fully, the lack of federal funding of hES cell research must be examined in the context of private funding. Private funding of biotechnology research is intimately related to the presence of patents covering the technology or products being developed.⁶⁵ A standard justification for the patent system is that investors will not fund private ventures without the incentives provided by patent protection.⁶⁶ Conversely, when trying to assess the effectiveness of the patent system at providing ideal incentives to innovators, one must consider other incentives, such as federal funding.⁶⁷

Application of these principles to the present hES cell research

61. See Easterbrook, *supra* note 43.

62. For example, Daniel Parry, executive director of the Alliance for Aging Research, an advocacy group that promotes stem cell research, stated, "The president's Aug. 9 speech managed to confound both sides. It was a temporary compromise that allowed voices on both sides to be calmed temporarily." Stolberg, *supra* note 51.

63. *Id.*

64. Clymer, *supra* note 51. Frank Bruni, *Bush Says He Will Veto Any Bill Broadening His Stem Cell Policy*, N.Y. TIMES, Aug. 14, 2001, at A1, available at www.nytimes.com/2001/08/14/politics/14BUSH.html; Chris Adams, *Congress Braces for Vigorous Debate on Bush's Stem-Cell Funding*, WALL ST. J., Aug. 31, 2001, at A10; Justin Gillis & Ceci Connolly, *Bush Policy on Stem Cells Appears Safe on Hill*, WASH. POST, Sep. 2, 2001, at A15. These hearings have been put on hold in light of the Sep. 11, 2001, attacks on the World Trade Center and the Pentagon.

65. It is true that there is a middle ground of research that is incentivized by both federal funding and patents. The prime example is universities, although companies sometimes also receive federal funds.

66. See generally Mark A. Lemley, *Reconceiving Patents in the Age of Venture Capital*, 4 J. SMALL & EMERGING BUS. L. 137 (2000).

67. John M. Golden, *Biotechnology, Technology Policy, and Patentability: Natural Products and Invention in the American System*, 50 EMORY L.J. 101 (2001) ("[T]he multi-billion dollar system of investment, mostly public and mostly university-based . . . provides most of the researchers and basic research that drives modern biotechnology."). *Id.*

environment suggests that the financing system for hES cell research has broken down. As described below, a single entity (WARF) owns the patent rights to hES cells, allowing it to control the direction of future research.⁶⁸ The looming presence of this strong property right along with the lack of federal funding results in diminished incentives for other researchers to develop therapies. Developments in hES cell technology will be inhibited.

1. AN INTRODUCTION TO PATENT DOCTRINES

The basis of U.S. patent law, as expressed in the Constitution, is to provide incentives to invent and create. One of the enumerated powers given to Congress is “[t]o promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries.”⁶⁹ With respect to inventions, Congress has implemented this power with statutes whose primary goal is to give inventors a limited “monopoly”⁷⁰ of roughly twenty years⁷¹ in exchange for disclosure of the invention. This bargain is realized in the structure of the patent. A patent consists of claims,⁷² which define the boundaries of the property right, and a disclosure, which provides a written description of the best mode⁷³ for making and using (“enabling”) the invention. To receive a property right, a patent applicant must contribute something to society. This requirement is formally set down in the requirements of usefulness,⁷⁴ novelty,⁷⁵ and nonobviousness.⁷⁶

The PTO and the courts attempt to ensure that the property right as

68. “Geron’s investments give it commercial rights to the research. Geron provided nearly all the funds that enabled Wisconsin researcher Jamie Thomson to discover human embryonic stem cells in 1998.” Elias, *supra* note 58.

69. U.S. CONST. art. I, § 8, cl. 8.

70. Monopoly is emphasized because the patent laws do not award a monopoly as it is known conventionally. As will be discussed *infra* Part III, patent property rights are typically narrower than the market power present in traditional monopolies. Moreover, future innovators may receive “blocking” patents for an innovation that makes a significantly better use of the first invention. In such a situation, the first patent holder will be forced to bargain with the second patent holder if she wishes to take advantage of the advances covered by the claims of the second patent.

71. See Drug Price Competition & Patent Term Restoration Act of 1984, 35 U.S.C. § 156 (2002). In the pharmaceutical field, a twenty-year patent in effect may be much shorter due to the length of time it takes to receive Food and Drug Administration (FDA) approval. There is an opportunity, however to extend the life of the patent by the length of time it took for the FDA to review the drug. *Id.*

72. See 35 U.S.C. § 112 (2002).

73. *Id.*

74. *Id.* § 101.

75. *Id.* § 102.

76. *Id.* § 103. Each of these doctrines will be discussed further *infra* Part III.

defined by the claims is only so large as the patent disclosure warrants.⁷⁷ Initially, a patent applicant submits an application to the PTO for examination. The PTO looks specifically for utility, novelty, and nonobviousness in the claims, and for enablement, written description, and best mode in the disclosure. Once the PTO deems these requirements satisfied, it issues the patent claims. Afterward, there is a short period of reexamination wherein the patent can be revoked.⁷⁸ Finally, a patent can be the subject of litigation. Typically, a patent holder sues a party for infringement of the patent claims. As a defense, the infringer argues that the patent claims are invalid: that the court should strike down the claims on the ground that the PTO erred in issuing them because they did not pass the requirements listed above.⁷⁹ Courts also define the scope of claims, when not invalidating them.⁸⁰ Thus, both the PTO and the courts play roles in defining the extent to which patent property rights are granted, and the scope of those rights.

The fundamental idea underpinning patent statutes, PTO examination, and case law is that, without the reward of a "monopoly," inventors would not invest the time or money to contribute new and useful things to society. A premise of this notion is that such inventions would not be contributed in the absence of the patent system. However, because the goal of the patent system is to provide incentives to innovate, patent law must be carefully calibrated so as not to concomitantly stifle invention; unwarranted monopoly power must be vigilantly guarded against. Although it may be true that patents are necessary to encourage innovation, they may also stifle it if the property rights awarded are too broad. One must always keep in mind the effect of a property right on subsequent innovators.

Failure to strictly adhere to patent doctrines results in patents that do not serve these policy goals well. For example, when property rights are awarded for a discovery that is not new, subsequent development of the discovery may be inhibited. One manifestation of this is the recent troubling issuance of property rights covering DNA sequences. Such patents are inappropriate based on patent doctrine: the sequence is not new (it is a product of nature) and not always immediately useful. Moreover, from a broader perspective, is the patent system promoting innovation overall when thousands of laboratories, physicians, and

77. See generally *infra* note 155.

78. See Allan M. Soobert, *Breaking New Grounds in Administrative Revocation of U.S. Patents: A Proposition for Opposition—And Beyond*, 14 SANTA CLARA COMPUTER & HIGH TECH. L.J. 63, 80-103 (1998).

79. One who fears that she may infringe a patent claim may only obtain a declaratory judgment if she can show that she is likely to be sued by the patent holder for infringement.

80. See *infra* note 155, at 840.

scientists must then pay for the right to study or use the DNA sequence to develop therapies? It is relatively clear that the PTO properly ignores such implications; the PTO is not suited to make economic analyses concerning the effects of a patent on an industry. Nonetheless, the PTO can continue to adhere to its practice of using patent doctrines without considering broad economic implications and avoid negatively affecting innovation, as long as it focuses on issuing only narrow claims that truly cover the inventive leap disclosed, and ensures that the invention is truly new. In this respect, the PTO and the courts should be careful before issuing or upholding patent claims to products, especially products of nature. This is only meant to be a short introduction to this subject. These ideas, as well as the patent doctrines set out by statute, will be discussed in more detail in Part III.

2. THE WARF PATENTS⁸¹

WARF holds patents (licensed from Dr. James Thomson) for the isolating and culturing method, as well as for the primate and human ES cells themselves as represented by the product claims.⁸² WARF's patents cover not only the cell-lines Dr. Thomson isolated, but all hES cells. The effect of this broad property right on subsequent innovation will be discussed extensively below.

Dr. Thomson's method required the destruction of human blastocysts in order to purify the pluri potent cells found in the inner cell mass. According to Dr. Thomson, the hES cells he described in his patent can remain in their pluri potent state—that is, they remain stem cells with the capacity to become most of the mature cells of the body—for over a year and can be coaxed into differentiating into different types of mature cells.⁸³ This feat—not the purification of the hES cells—represents the inventive step contributed by Dr. Thomson. Scientists, long aware of the existence of ES cells,⁸⁴ had been searching for years for ways to keep them alive in their pluri potent state in petri dishes (in “culture”) in such a way that they retained their ability to differentiate into the various mature cells of the adult body.⁸⁵ Dr. Thompson “credited his success in part to the recent availability of new nutrient broths that have made it

81. There are also other less broad patents: U.S. Pat. Nos. 5,874,301 (issued Feb. 23, 1999) & 5,914,268 (issued June 22, 1999) (held by the National Jewish Center for Immunology and Respiratory Medicine); U.S. Pat. No. 5,453,357 (issued Sep. 26, 1995) (held by Vanderbilt University).

82. Associated Press, *Where the Stem Cells Are*, Aug. 27, 2001. See also *infra* Part I.D.3.

83. U.S. Pat. No. 6,200,806, *supra* note 4.

84. See Weiss, *supra* note 21.

85. *Id.*

easier to grow human embryos up to⁸⁶ the blastocyst stage. Although this method represents the inventive leap, WARF was able to obtain the following two broad product claims.

a. The Primate Patent Product Claim

Claim 1. A purified preparation of primate embryonic stem cells which (i) is capable of proliferation in an in vitro culture for over one year, (ii) maintains a karyotype in which all the chromosomes characteristic of the primate species are present and not noticeably altered through prolonged culture, (iii) maintains the potential to differentiate into derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and (iv) will not differentiate when cultured on a fibroblast feeder layer.⁸⁷

b. The hES Cell Patent Product Claim

Claim 1. A purified preparation of pluripotent *human* embryonic stem cells which (i) will proliferate in an in vitro culture for over one year, (ii) maintains a karyotype in which the chromosomes are euploid and not altered through prolonged culture, (iii) maintains the potential to differentiate to derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and (iv) is inhibited from differentiation when cultured on a fibroblast feeder layer.⁸⁸

3. IMPLICATIONS OF WARF'S ES CELL PATENTS

The ES cell patents cede a remarkable amount of territory to WARF. In effect, WARF has staked out an interest in, as well as the possibility of controlling, all future hES cell research and product development, regardless of how or from where the hES cells are derived.⁸⁹ Carl Gulbrandsen, WARF's managing director, has interpreted these claims to apply "to any cell that is derived from a human embryo and continues to thrive and multiply without specializing."⁹⁰ By this rationale, even though others might develop different methods of preparing hES cells, they still must deal with WARF before using them.⁹¹ One

86. *Id.*

87. U.S. Pat. No. 5,843,780, *supra* note 4. Note that there are method claims.

88. U.S. Pat. No. 6,200,806, *supra* note 4 (emphasis added). Note that there are method claims.

89. N. Zeke Campfield, *U. Wisconsin: Stem-Cell Research Places U. Wisconsin in National Spotlight*, *BADGER HERALD*, Aug. 31, 2001, available at 2001 WL 24685338. And "as inventors and owners of the patent for the human embryonic stem cell, owners of five of the reported 64 cell lines in existence and with other scientists unable to create new cell lines, UW is now a major player in the future of this new science." *Id.*

90. *Id.*

91. "WARF believes that virtually all of the other embryonic cell lines now in existence come under the Thomson patent and cannot be imported into the United States for use by NIH

implication this scenario is that if doctors prepare hES cells from a person as part of the process of making immuno-compatible tissues or organs, they will infringe the patent claim. Gulbrandsen adds that “distributors of all human embryonic stem cell lines will need a license from WARF.”⁹² Not only may WARF control who uses hES cells in the United States, but it may also control their research and development agenda.⁹³

The WARF patents and President Bush’s decision may combine to lethally block subsequent research. First, from an intellectual property perspective, WARF’s claims may have been strengthened by President Bush’s decision. The WARF patent product claims are very broad even in the absence of President Bush’s decision.⁹⁴ His decision can only contribute to their breadth because without federal funding fewer scientists will be able to work in the field.⁹⁵ Additionally, in the absence of competing research the chances of creating future innovations that may block, compete with, or “invent around” the use of the hES cell-lines in existence before President Bush’s speech become marginal.⁹⁶

Second, the value of the WARF patents, especially in combination

researchers unless they are licensed by WARF.” Paul Recer, *Bush Challenged on Stem Cells* (on file with author). However, note that Geron reported preparation of ES cells without using feeder cells, a limitation that is explicitly stated in the WARF patent claims. Xu et al., *Feeder-free Growth of Undifferentiated Human Embryonic Stem Cells*, 19 NATURE BIOTECHNOLOGY 971 (2001). See also *Cell Cultures: Breakthrough in Scalable Growth of Human Embryonic Stem Cells Achieved*, GENOMICS & GENETICS WEEKLY, Nov. 16, 2001, at 18, at NewsRx.com.

92. Aaron Nathans, *UW, NIH Reach Deal on Stem Cells: WARF Will Allow Widespread Nonprofit Research*, WIS. ST. J., Sep. 6, 2001, at 2A, available at 2001 WL 25524490.

93. Sheryl Gay Stolberg, *Patent Laws May Determine Shape of Stem Cell Research*, N.Y. TIMES, Aug. 17, 2001, available at www.nytimes.com/2001/08/17/politics/17CELL.html. “[T]he foundation has granted important rights to . . . Geron . . . , giving that company considerable say over who ultimately profits from stem cell therapies.” *Id.* “People complain about OPEC being a monopoly, but even they have eleven members.” Center for Science, Technology, & Congress at the American Association for the Advancement of Science, *supra* note 3, at 30 (quoting Senator Edward Kennedy, Chairman of the Senate Health, Education, Labor, and Pensions Committee, commenting on WARF’s hold on ES cell research).

94. “There’s never been a scientific project in the history of humankind that was owned this far [upstream] . . . for WARF to own the actual stem cell lines is as close to patenting NATURE as you can get.” Julia Brunts, *Now Embryonic Stem Cell Research Faces Tests in Legal Sphere*, CHI. DAILY L. BULL., Aug. 20, 2001, at 1 (quoting bioethicist Glenn McGee).

95. “No one got luckier [after Bush’s decision] than UW researcher James Thomson, who has quickly risen to fame—his face even appeared on the cover of Time magazine.” Campfield, *supra* note 89; see also James Kelly, *Our Scientific Method*, TIME, Aug. 20, 2001, at 4.

96. “Bush’s decision may have strengthened the hands of the [WARF] and Geron. By refusing to allow taxpayer money to finance creation of new cell lines in this country, Mr. Bush reduced the chances that scientists would derive and patent cells that might challenge Wisconsin’s dominance in the field.” Stolberg, *supra* note 93. Additionally, “researchers in other countries have a double advantage [because] other nations, notably Britain, have fewer restrictions on studies of human embryos” and they need not worry about infringing the U.S. patent. *Id.*; see also Brunts, *supra* note 94.

with President Bush's decision, cannot be overstated.⁹⁷ Academic scientists now must sign licensing agreements with WARF and those who owned hES cells prior to August 9, 2002, if they wish to conduct their research consistent with President Bush's decision.⁹⁸ Any such agreement will undoubtedly award commercialization rights to any discovery made by the licensee to the licensor.⁹⁹ Private companies will likely wisely devote their energy and capital to other lines of research. Some,

97. For example, four days after President Bush's decision, WARF sued Geron in an attempt to block it from exercising an option giving it control of all of WARF's stem cell lines. The suit was amended on September 25, 2001. David P. Hamilton, *Geron Faces Further Complaints in Suit by Stem-Cell Patent Owner*, WALL ST. J., Sept. 26, 2001, at B2, available at 2001 WL-WSJ 2876589. Geron had obtained exclusive rights from WARF to develop ES cells into liver, muscle, nerve, pancreas, blood, and bone cells. Stolberg, *supra* note 93. Geron's exclusive licenses to the WARF patents "might mean that anyone seeking to develop commercial applications of stem cells must negotiate with Geron first." *Id.* WARF and Geron settled in January, 2002. Andrew Pollack, *University Resolves Dispute on Stem Cell Patent*, N.Y. TIMES, Jan. 9, 2002, at C11. The agreement gives Geron exclusive commercial rights to neural, heart, and pancreatic islet cells, and non-exclusive rights to commercially develop treatments based on bone, blood, and cartilage cells.

98. After President Bush's decision, DHHS Secretary Tommy Thompson's first priority was to ensure that WARF would not use its patent to block access of basic researchers to the putative sixty-four cell lines mentioned by President Bush. A deal was reached on September 4, 2001. Memorandum of Understanding, Embryonic Stem Cell Research at the University of Wisconsin-Madison, available at <http://www.news.wisc.edu/packages/stemcells/index/msql?get=6458>; Laura Meckler, *Deal Made in Stem Cell Patent Issues* (on file with author). The deal permits NIH scientists to publish their research results. Additionally, "NIH will retain ownership to any new intellectual property that might arise from the conduct of its research in this area." *Wicell Signs Stem Cell Research Agreement, Embryonic Stem Cell Research at the University of Wisconsin-Madison*, at <http://www.news.wisc.edu/packages/stemcells/index.html>. Nevertheless, Wisconsin retains commercial rights to its materials. "The use of the patent rights, the agreement states, will be for teaching or non-commercial research only. The Wisconsin patent rights do not cover commercial applications arising from research using the cells Such commercial applications would require a separate written agreement with WiCell or WARF." Ron Seely, *Stem-Cell Pact Will Give Scientists Easy Access to UW Lines WARF-NIH Agreement Touted as a Commitment to Widespread Distribution of the Cells*, WIS. ST. J., Sep. 6, 2001, at A1, available at 2001 WL 25524423. According to WARF's spokesman, WARF is "providing the cells for research purposes. If commercial applications are done, [the users] would have to contact [WARF]. It's a very complicated process." Nathans, *supra* note 92. "Profits will come once stem cell research yields products, drugs, or treatments that can be commercialized, like a treatment to replace the need for insulin for diabetics, WARF officials have said." Katherine M. Skiba & Marilyn Marchione, *UW Cells Cleared for Research*, MILWAUKEE J. SENTINEL, Sept. 6, 2001, at A01, available at 2001 WL 27403434. In addition, the agreement requires "other stem-cell providers to negotiate with the foundation should they enter commercial agreements with university researchers." Laurie McGinley et al., *White House Cuts Estimate of Available Stem Cells*, WALL ST. J., Sept. 6, 2001, at A2, available at 2001 WL-WSJ 2874725. The "specific terms and conditions and availability must be determined between providers of the cells and the recipients" Kim Coghill, *Administration Enters Deal with Owners of Stem Cells*, BIOWORLD TODAY, Sep. 6, 2001, available at 2001 WL 7295637. "Each will have to come to an individual agreement with" Wisconsin. Nathans, *supra* note 92. The deal "applies only to government-employed scientists, and covers only basic research; if scientists want to use the cells as therapies, then they will have to renegotiate." Sheryl Gay Stolberg, *U.S. Concedes Some Cell Lines Are Not Ready*, N.Y. TIMES, Sept. 6, 2001, at A1, available at 2001 WL 27395101.

99. "If new drugs or other commercial therapeutics are developed from the research, the

although not all, academic researchers might feel the same way. For example, biologist Douglas Melton of Harvard University proclaimed that WARF/Geron's "conditions would mean that I am the ideal employee of Geron. They don't pay my salary, they don't pay my benefits, but anything I discover they own."¹⁰⁰ Additionally, even if academic researchers decide that they do not mind being pseudoemployees of WARF/Geron, they will have to find private sources of funding and isolate all hES cell work from the rest of their laboratory, just as Dr. Thomson did. The theoretical bases of these problems will be discussed in Part II.

II. DOES THE ISSUANCE OF PROPERTY RIGHTS TO BROAD UPSTREAM DISCOVERIES OR INVENTIONS BEST PROMOTE THE SPEED OF BIOTECHNOLOGY INNOVATIONS?

ES cells can be thought of as a basic research tool,¹⁰¹ an upstream,¹⁰² pioneering-type discovery,¹⁰³ or both. Either characterization reveals their importance in future biotechnology research and the relevance of issuing property rights to them. Although the possibility of obtaining claims that give broad property rights to such a basic, upstream, pioneering technology certainly will motivate entrepreneurs to

license owners could stand to gain millions of dollars." Toni Clark, *Geron Sued by Researchers over Stem Cell Rights* (on file with author) (Aug. 14, 2001).

100. Stolberg, *supra* note 93. Dr. Melton has apparently decided to ignore the patent and derive new stem cells from embryos obtained from a local IVF clinic. Reuters, *Harvard Scientist Pursues New Stem Cell Research* (Sep. 5, 2001) (on file with author). He intends to distribute them to anyone who needs them for research purposes. "They are not being prepared with the intention of having any rights, commercial or otherwise." NewsRx.com & NewsRx.net, *Harvard University: Fertility Clinic to Give Embryos to Harvard University for Research in Major Deal*, BIOTECH WEEK, Sept. 12, 2001, at 16, available at 2001 WL 17569221. Similarly, Israeli researchers say "they have begun shipping human embryonic stem cells to outside labs . . . without permission from" WARF. Dan Vergano, *Stem Cells from Israel Are Sent to Harvard Lab*, USA TODAY, Sept. 5, 2001, at 2A. The Israeli lab "says because it is outside the USA and because its scientist collaborated with the Wisconsin researcher who holds the patent, it doesn't need the foundation's permission to distribute the lines." *Id.*

101. Research tools are anything that assist a scientist in discovering a drug or other type of therapy. A research tool can be thought of as a final product if it is marketable. See Rebecca S. Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017, 1066-67 (1989). Alternatively, a research tool may be thought of as an intermediate step in the process of developing the final product. The "general issue of patents over research tools has become a very controversial issue." Brenda Sandberg, *The Hard Cell: A Move into the Midwest Gives Heller a Piece of Hot Litigation in the War over Stem Cell Research*, RECORDER, Aug. 23, 2001, at 1 (quoting patent attorney Lynn Pasahow).

102. See discussion *infra* Part II.A.1. (defining upstream and downstream inventions). Arti Rai defines upstream research as "research that is relatively far removed from a commercial end product." Arti K. Rai, *Fostering Cumulative Innovation in the Biopharmaceutical Industry: The Role of Patents and Antitrust*, 16 BERKELEY TECH. L.J. 813, 816 (2001).

103. See discussion *infra* Part II.A.2. (defining pioneering invention).

innovate, what effect does the existence of such claims have on subsequent innovators? The specific issue that will be addressed by this article is whether WARF's broad upstream patent claims could dissuade other companies from investing in hES cell research and therapy development.¹⁰⁴ At least one study suggests that granting broad claims does not increase overall research and development or innovative output.¹⁰⁵ When upstream research is controlled by a single firm for the duration of the patent term, other firms must resort to negotiations in order to work in the same field.¹⁰⁶ Negotiations might be unsuccessful for many reasons, a chief one being the superior bargaining power bestowed upon the patent holder by the patent system. High transaction costs could stifle research.¹⁰⁷

In this scenario, a patent claim covering "basic research material—as opposed to a final product—reduces the commercial incentive to fund research because the original patent holder could be entitled to anything from royalty fees to patents covering a new invention or discovery."¹⁰⁸ In economic terms, the patent holder is seeking a rent. For example, in the extreme, rent seeking can take the form of cybersquatting, in which people who do nothing to deserve a property right can demand large sums of money to release it. Patents covering genes and hES cells may be more justifiable, but only slightly so. Dr. Thomson discovered a way to keep hES cells alive in culture for a year in such a way that they can be manipulated to transform into many of the mature cells in the human body. He has not yet shown exactly how these cells can be used or the

104. While it is true that patents are issued to private firms to provide incentives to invest in expensive research and development, "stem cells are another issue because of the danger that not enough researchers will have access to the cell lines for all of the scientific possibilities to be fully explored." Brunts, *supra* note 94. Moreover, patent applications directed at human embryonic cells and embryos are dramatically increasing. Amy Outchet, *Putting Embryos on the Assembly Line*, UNESCO COURIER, Apr. 1, 2001, at 38. Geron "has filed about 30 new patent applications for the various techniques and technologies it uses." Associated Press, *Seeking Profit in Stem Cells*, WIRED, July 13, 2001, at www.wired.com/news/print/0,1294,45232,00.html. Geron "has applied for about 40 more patents involving stem cells." Elias, *supra* note 58.

105. Mariko Sakakibara & Lee Branstetter, *Do Stronger Patents Induce More Innovation? Evidence from the 1988 Japanese Patent Law Reforms*, 32 RAND. J. ECON. 77,100 (2001), available at 2001 WL 21701359.

106. See Rai, *supra* note 102, at 816.

107. Indeed, "[a]t least one university has backed out of licensing talks with Geron, complaining that the company wanted too high a price for access to its stem cells." Neil Munro, *Next Battle in the Stem-Cell War*, NAT'L J., Sept. 1, 2001, available at 2001 WL 25926063.

108. Brunts, *supra* note 94.

A company may receive broad powers over simply retrieving embryonic stem cells or culturing and guiding them in a particular direction. This is not to suggest that such feats do not require ingenuity. Yet depending upon the scope of the patent awarded, we could see a re-run of the same abusive pay-per-view approach taken with genes.

Outchet, *supra* note 104.

best and safest methods for using them. Indeed, it is clear to all scientists that years of research remain before the full potential of hES cell-derived therapies will be realized. Dr. Thomson, just like the discoverers of genetic sequences, did some important work to contribute to the knowledge base, but the question is whether the initial, relatively minimal amount of work he did should entitle him to control future research and development of hES cells and possible therapies.

These concerns are particularly important in fields that are technologically immature and scientifically unclear. Indeed, it is clear that while the WARF patents might represent roadblocks to investment, a similarly important impediment is the simple fact that the scientific principles underlying the use of hES cells are not fully understood.¹⁰⁹ Now is the time that scientists should be encouraged to provide insight, effort, and resources into discovering how hES cells function and can be manipulated. Scientific research, especially in fields that benefit from creativity, is a cumulative, synergistic process that relies on the input of many varied researchers and their corresponding diverse views. Restricting those views will slow the pace of innovation. Indeed, serendipitous results may amount to breakthroughs. The probability of discovering useful serendipitous results increases with the prevalence of incentives for researchers to carry out the research. More intellectual property protection may not help increase the rate of innovation in fields of inquiry that require imagination.¹¹⁰ Part II addresses this issue.

The stifling effect of such broad patent claims is amplified in the case of hES cells due to the desire of politicians to regulate hES cell research. Nevertheless, our political system should retain its goals of providing incentives for the development of therapies. Technologies in their infancy, such as hES cell research, require support from all direc-

109. *Stem Cells: Potential for Good?*, *supra* note 17.

Mother Nature, more than government money, is the biggest obstacle to stem-cell therapies. For all the publicity, stem cells are for the most part still stuck in the laboratory. Getting them to the patient is going to take not only much more research to demonstrate their safety and efficacy in treating disease, but also considerable commercial creativity to turn these laboratory marvels into profitable products.

Id.

110. See Comments of Professor Joseph Farrell of University of California, Berkeley Economics Dept. in FTC/DOJ hearings at the Haas School of Business, Feb. 28, 2002 (on file with author). For example, in the computer industry where it is clear that the goal is the increase of microprocessor speed, strong intellectual property protection might be appropriate because allowing a single firm to control the obvious direction of research is more efficient, and the development is expensive. Conversely, in fields requiring many creative, perhaps sometimes serendipitous, inputs of lower expense, strong intellectual property rights are more problematic. Professor Farrell also suggests that strong intellectual property rights are problematic in areas with few alternatives, as is true for ES cell research (that is, there is no other hES cell than that covered by the WARF patents.)

tions. Because so little is understood about the scientific principles underlying hES cells, many diverse viewpoints need to be supported and heard. Federal funding will provide such incentives. In the absence of federal funding, the lure of obtaining a patent may provide similar incentives, but the presence of a dominating, all-encompassing patent will dissuade non-patent holders. The remainder of this Part will begin with a discussion of policy considerations useful for analyzing whether the hES cell patent product claims provide the desired incentives for innovation. Parts III and IV will address possible legal means for implementing desirable policy.

This Part begins with the status of hES cell research: can the present technology be characterized as upstream or downstream, as basic or applied, as a pioneering or governing innovation, or as commercializable technology? This Part will then turn to an analysis of whether the incentive goals of patent law are served by granting a property right to an upstream or basic research discovery.

A. *Characterization of the Invention Described in the WARF Patents*

1. THE PROBLEM OF DISTINGUISHING UPSTREAM OR BASIC RESEARCH FROM DOWNSTREAM OR APPLIED SCIENCE IN BIOTECHNOLOGY

In general for the purposes of biotechnology, basic research can be considered upstream, while applied technology can be considered downstream. It is extremely difficult to distinguish between upstream/basic research and downstream/applied science in biotechnology.¹¹¹ In the biopharmaceutical (biotechnology and pharmaceutical) industry the crowning achievement typically is a marketable drug. Note, though, that years of research by a single company, based on decades of work done by other researchers around the world, involving hundreds of millions of dollars (just in the final stages) is required to discover and develop the final product.¹¹² During this pre-drug phase, because so many different techniques and chemical and biological compounds are used to develop the drug, pre-drug discoveries might turn out to be useful as marketable research tools. Such tools might be sold to other companies or laboratories to help them in their quest to discover drugs. Indeed, there are companies whose business model is to develop only such research tools. Thus, it becomes very difficult to discern when a biological discovery is a "final product" or an upstream discovery. For example, "research identifying a gene linked to a disease might be quite 'upstream' if the

111. See John M. Golden, *Biotechnology, Technology Policy, and Patentability: Natural Products and Invention in the American System*, 50 EMORY L.J. 101, 118-19 (2001).

112. Rai, *supra* note 102, at 815 n.4.

commercial goal is a drug therapy. By contrast, if the commercial goal is a diagnostic test, research identifying the gene might be relatively 'downstream.'¹¹³ Further complicating the issue is the fact that the patenting and commercializing of upstream, basic research is promoted both by the government¹¹⁴ and capital markets.¹¹⁵ In other words, basic research in such a cumulative field has commercial applications.

Nevertheless, a rough distinction is suggested by Professor Rebecca Eisenberg. Basic research would include research that "leads down unexpected paths for which a course cannot be charted in advance, and [whose] success . . . depends on insights and creativity that may differ from one investigator to the next."¹¹⁶ By contrast, applied research would be research that is "a matter of systematic trial and error, in which the insights and creativity of individual investigators play little if any role."¹¹⁷ Although this distinction may not help define many innovations such as research tools, it can be applied relatively easily to hES cells. Presently, scientists are at the very beginning of recognizing the possibilities of the hES cell. The patent holders have not demonstrated an immediately useful therapeutic use for hES cells, and the only commercial use demonstrated is the sale of human-made unique cell-lines to other researchers. It is certainly not at a stage consisting of uncreative, systematic trial and error research. Any application, commercial or not, remains to be discovered, characterized, and successfully implemented. It is reasonable to place hES cell research back toward the basic-research side of the basic research-applied science continuum. At this stage, the ES cell patents are most appropriately characterized as covering upstream/basic research.

The importance and difficulty of characterizing research as upstream/basic or downstream/applied is illustrated by two sometimes

113. *Id.* at 816 n.9 (discussing how basic research may be thought of as "upstream" while the activities nearer to the final production of a product, for example, a drug, may be thought of as downstream).

114. See discussion of the Bayh-Dole Act, *infra* text accompanying notes 118-25.

115. "Modern techniques in biotechnology have 'accelerated the commercial development of basic research discoveries and attracted commercial interest in academic biomedical research in its early stages.' Biotechnology firms and academia have formed hundreds of strategic alliances." Yusing Ko, *An Economic Analysis of Biotechnology Patent Protection*, 102 YALE L.J. 777, 794 (1992).

116. Eisenberg, *supra* note 101, at 1066-67.

117. *Id.* at 1067. "[A] user's research tool may be a provider's end product. Some products that are currently used in research might also have markets, actual or potential, among nonresearch consumers." Rebecca S. Eisenberg, *Bargaining over the Transfer of Proprietary Research Tools: Is this Market Failing or Emerging?*, in EXPANDING THE BOUNDARIES OF INTELLECTUAL PROPERTY: INNOVATION POLICY FOR THE KNOWLEDGE SOCIETY 223, 228 (Rochelle Cooper Dreyfuss et al. eds., 2001).

competing patent policies: the Bayh-Dole Act's¹¹⁸ promotion of patenting of upstream/basic research discoveries, and the prohibition of patenting products of nature.¹¹⁹ The Bayh-Dole Act allows recipients of government funding (generally academic scientists) to patent and license inventions that were developed using government money.¹²⁰ Bayh-Dole emanated from a cooperative model of research and development between academia and industry and "epitomized the newfound confidence in strong intellectual property rights as the route to quick and cheap commercialization."¹²¹ The idea was to provide "incentives for American scientists to assist in the first stages of converting their discoveries to commercial use."¹²²

But has Bayh-Dole unwisely promoted the patenting of upstream or pioneering basic research? Afterall, academic researchers generally study upstream/basic research subjects. Because of the lack of a control, it is not possible to clearly discern what Bayh-Dole's impact has been.¹²³ Nevertheless, "[o]ne study of academic basic research identified 'intellectual property' as the third major function of the university."¹²⁴ Thus, whether it is because of Bayh-Dole or not, universities are major participants in the patent system. Moreover, because universities are the home of basic biomedical research, upstream/basic research is being patented at a greater rate than ever.¹²⁵

118. 35 U.S.C. § 200 (2002).

119. See *infra* Part III:A.I. for discussion of this doctrine.

120. Tamsen Valoir, *Government Funded Inventions: The Bayh-Dole Act and the Hopkins v. CellPro March-In Rights Controversy*, 8 TEX. INTELL. PROP. L.J. 211, 213 (2000). The Act attempts to increase innovation by "encouraging the participation of small business firms and promoting the public availability of inventions, yet ensuring that the government obtains sufficient rights in federally supported inventions to meet the needs of the government and the public." *Id.*

121. Golden, *supra* note 111, at 120.

122. *Id.* at 121. Other laws passed in this spirit include the Federal Technology Transfer Act of 1986, Pub. L. No. 99-502, 100 Stat. 1785 (1986) (codified as amended at 15 U.S.C. §§ 3701-3714 (Supp. III 1998)), and the National Cooperative Research Act of 1984, Pub. L. No. 98-462, 98 Stat. 1815 (1984) (codified as amended at 15 U.S.C. §§ 4301-4305 (1994)) (reducing antitrust enforcement for firms performing collaborative research).

123. There is some data, however. For example, there has been a five-fold increase in industry funding of university research, and a ten-fold increase in the number of licenses granted by universities since Bayh Dole's enactment. Valoir, *supra* note 120, at 234. Moreover, there has been a four-fold increase in royalties paid to universities between 1981 and 1992, and a doubling between 1991 and 1995. *Id.* The "number of university-issued patents increased [ten times since the passage of Bayh-Dole] from 220 in 1979 to 1148 in 1989 to 3024 in 1998," compared to a three-fold increase in the number of patents issued to industry over the same period of time. *Id.* (citations omitted). There has also been an increase in patent litigation involving universities. Jennifer Polse, *Holding the Sovereign's Universities Accountable for Patent Infringement after Florida Prepaid and College Savings Bank*, 89 CAL. L. REV. 507, 527 (2001).

124. Clarisa Long, *Patents and Cumulative Innovation*, 2 WASH. U. J.L. & POL'Y 229, 243 (2000).

125. See *supra* note 123.

In contrast, the policy behind prohibiting the patenting of products of nature supports leaving basic discoveries in the public domain, that is, not dispensing property rights covering them. This doctrine holds that something that exists in nature, even if previously unknown to humans, may not be patented.¹²⁶ The wisdom of this doctrine lies in part in the fact that products of nature often constitute elements of basic biotechnology research. For example, as discussed above, both hES cells and the method of isolating them constitute upstream/basic research. Decades of discoveries, innovations, and inventions remain in determining how hES cells may be utilized. It is impossible to predict how the basic research will be used to invent and innovate. The product-of-nature prohibition on patentability strives to avoid impeding development of practical uses stemming from basic research. In the present environment of encouraging patenting and commercialization of upstream research, the product-of-nature doctrine is one mechanism for the PTO and the courts to “ensure that the gain that comes from spurring private investment is greater than the loss that results from slowing science or increasing its cost.”¹²⁷ The Bayh-Dole Act and the product-of-nature doctrine illustrate the difficulty the legal system faces when characterizing discoveries as upstream or downstream and deciding how to best promote subsequent development of upstream discoveries and innovation of downstream discoveries.

2. THE PROBLEM OF DETERMINING WHAT IS A “PIONEERING” INVENTION AND WHAT IS AN “IMPROVEMENT”

It is also useful to analyze patents on the basis of whether the invention described is “pioneering” with respect to the field, or is an “improvement” of a pioneering invention. These terms typically are not directly important for the PTO in determining whether a patent claim should be issued, but they do help in trying to understand the implications of the issuance of a patent claim on subsequent development.¹²⁸ This article argues that it is unwise to give property rights to pioneering inventions that are too undeveloped, when the crucial technological advances are improvements.

According to the Supreme Court, a pioneer patent is “a patent covering a function never before performed, a wholly novel device, or one of such novelty and importance as to mark a distinct step in the progress

126. See discussion *infra* Part III.

127. Golden, *supra* note 111, at 164-65 (citations omitted).

128. Additionally, they sometimes play a role in infringement cases; a court may overlook infringement of a claim if the infringing invention is pioneering. *Westinghouse v. Boyden Power-Brake Co.*, 170 U.S. 537, 561-62 (1898); see also *infra* Part III.A.4 (discussing the reverse doctrine of equivalents).

of the art, as distinguished from a mere improvement or perfection of what had gone before."¹²⁹ But what exactly is a "distinct step in the progress of the art"? What is a "mere improvement"? Distinguishing between the two—and determining which is more important—is especially difficult in fields of cumulative development. This debate goes back to at least the 1850s. For example, the designer of the Great Western Railway and the Great Eastern steamship stated that "the most useful inventions and improvements . . . are mere progressive steps in a highly wrought and highly advanced system suggested by, and dependent on, other previous steps, their whole value and the means of their application probably dependent on the success of some or many other inventions."¹³⁰ This is an apt description of the biopharmaceutical field.

It might seem appropriate to take into account the economic impact of an invention when attempting to characterize it as a pioneering or improvement invention, but the commercial, practical, or social ramifications of the invention theoretically are not considered when determining its pioneer status.¹³¹ Instead, the courts simply apply standard patent analysis to determine how different the invention is from the prior art.¹³² "Courts have considered an invention to be a pioneer when it presents a 'broad breakthrough,' 'major advance,' or 'basic operational concept'; or is 'broadly new' or 'devoid of significant prior art.'"¹³³ It is probably wise for the courts to attempt to avoid looking at commercial success.¹³⁴ Commercial success does not necessarily equate with pioneering status. For example, some truly pioneering inventions may not be suitable for marketing, whereas a minor improvement may result in commercialization. In fact, commercial success is probably more attributable to improvements. Put another way, a likely scenario is the following: a pioneering invention is not marketable as it represents the earliest stage

129. *Id.* The genesis of the pioneer invention doctrine is found in *Evans v. Eaton*, 20 U.S. 356 (1822). See also *Morley Sewing Mach. Co. v. Lancaster*, 129 U.S. 263 (1889) (discussing the use of the pioneer invention doctrine in an infringement case).

130. HENRY PETROSKI, *THE EVOLUTION OF USEFUL THINGS* 45 (1992). This inventor concluded that the patent system obstructs progress because "'really good improvements are not the result of inspiration,' but 'more or less the results of an observing mind, brought to bear upon circumstances as they arise, . . . [and because] . . . 'most good things are being thought of by many persons at the same time.'"*Id.*

131. John R. Thomas, *The Question Concerning Patent Law and Pioneer Inventions*, 10 HIGH TECH. L.J. 35, 48-49 (1995).

132. The "sole index of pioneer status . . . is the position occupied by the invention in its technological field." *Id.* "For an invention to be considered a pioneer . . . it must meet what amounts to a test of extraordinary nonobviousness." *Id.*

133. *Id.* (citations omitted).

134. This may be unavoidable; commercial concerns are often disguised as obviousness questions (pursuant to 35 U.S.C. § 103) such as the secondary considerations of *Graham v. John Deere*, 383 U.S. 1 (1966), including, for example, whether there is a need for the invention or whether others had failed at achieving it. *Id.* at 17-18.

of development; subsequent small improvements add to the invention making it more easily used by consumers and thus more economically valuable; a subsequent "radical improvement"¹³⁵ may render the invention altogether different, and thus might actually qualify as a pioneering invention. This scenario illustrates the difficulty of characterizing inventions in cumulative fields, especially when attempting to do so using commercial success or marketability as a metric.

Just as the invention described in the hES cell patents is most appropriately described as basic research, it also may be characterized as a pioneering invention. First, culturing the cells in such a way that they retain their ability to transform into mature cells was a "function never before performed, . . . one of such novelty and importance as to mark a distinct step in the progress of the art."¹³⁶ Second, standing by itself, the culturing technique is only commercially viable to the extent that it can be licensed to other laboratories; to develop into a marketable therapy, the patented invention needs "improvements." The quickest way to commercialize the technology will be to make and sell unique hES cell-lines—a downstream invention. In fact, WARF did this and is charging \$5,000 for a sample of a cell-line.¹³⁷ However, this improvement is not what was patented; rather, WARF patented all hES cells. Another downstream commercial application or improvement will be the use of the method of isolating and culturing the ES cells as part of a process of generating organs and tissues. Again, WARF did not patent this application. WARF patented its culturing method, a necessary stepping stone to both inventions; neither can be performed without invading the territory covered by the WARF claims. Any improvements will build on WARF's pioneering claims.

Considering both of these examples of downstream innovations, it becomes clear that the WARF claims represent a pioneering invention. The scientific community correctly lauds the technological leap made by Dr. Thomson. However, just because an improvement invention is made possible by an important pioneering scientific advance does not mean the pioneering inventor should obtain the right to exclude all future innovators from developing the technology. The following section addresses this issue.

135. "A radical—as opposed to 'ordinary'—improver builds on a pioneer's contribution, but in a very significant way: The improvement is the source of very high profits, as opposed to the pioneer's substantial but much lower profits." Robert Merges, *Intellectual Property Rights & Bargaining Breakdown: The Case of Blocking Patents*, 62 TENN. L. REV. 75, 79 (1994). Again, it seems that economic considerations enter into the analysis when attempting to define the invention, even though courts attempt to avoid this.

136. *Boyden Power-Brake Co. v. Westinghouse*, 170 U.S. 537, 561-62 (1898).

137. Nathans, *supra* note 92.

B. *Should Strong Property Rights Be Granted for Pioneering, Upstream, or Basic Research Biotechnology Discoveries?*

1. SHOULD THE PIONEER BE FAVORED BY THE PATENT SYSTEM IN THE RACE TO COMMERCIALIZE?

Why does the patent system award broad property rights covering not yet fully commercializable upstream pioneering inventions, as it did for the hES cell discovery? Some economic theorists support granting strong property rights to a pioneer inventor. For example, Edmund Kitch set forth his prospecting theory,¹³⁸ which holds that a patent system promotes efficient development of technologies only if it tends to assure efficient allocation of the resources among the prospects at an efficient rate and in an efficient amount, that management of each prospect is in the hands of the entity best equipped to manage it, and that information found by one entity is communicated to other firms at an efficient rate.¹³⁹

The patent system, according to Kitch, exists to promote proper exploitation of an invention. Under the prospect theory, pioneer patents are desirable because they allow a single firm to control and coordinate the development of the invention. For this to be true, that firm must be able to recognize and support all possible desirable developments. Additionally, transaction costs for bargaining with other firms must be minimal.

Kitch argued that the practice of granting broad patent claims long before the invention is commercially viable supports his theory.¹⁴⁰ This is particularly true in the context of biopharmaceutical patents where a patentee need only demonstrate a single use to receive a property right covering all uses.¹⁴¹ In other words, because so much development remains after the initial discovery of a pharmaceutical compound (for example, clinical trials), the patent permits the coordinated and efficient development of the product.

Joseph Schumpeter also focused on the development—what he called “innovation”—of the invention after its initial discovery.¹⁴² His notion that the invention prior to development results in “no economi-

138. Edmund W. Kitch, *The Nature & Function of the Patent System*, 20 J.L. & ECON. 265 (1977). A prospect is “a particular opportunity to develop a known technological possibility.” *Id.* at 266. This prospect theory is contrasted with the “reward theory” which holds that patents exist to compensate and reward the inventor for his investment in the creation. *Id.*

139. *Id.* at 266.

140. *Id.* at 267-68.

141. *Id.* at 269. Kitch points out that this does not conform to the traditional incentive theory of patent law.

142. JOSEPH A. SCHUMPETER, *BUSINESS CYCLES* 84 (1939); see also JOSEPH A. SCHUMPETER, *CAPITALISM, SOCIALISM, & DEMOCRACY* 81-110 (3d ed. 1950).

cally relevant effect at all” seems particularly prescient when considering to the hES cell patents.¹⁴³ However, Schumpeter used this insight to maintain that such inventors need patent protection in order to innovate.¹⁴⁴ Underlying this conclusion is the premise that a single coordinating firm is more suited to innovating than many independent freely contracting firms.

In practice, it is obvious why parties desire broad patent claims. First, the expense of applying for a patent must be justified by the value of the patent. Second, more intellectual property is awarded to a patentee by broader claims. This allows such a patentee to force others out of the field or to license from the patent holder the technology covered by the claims. The ability to obtain broad patent claims will have strong implications for the success of the company that holds the patent, while it may harm other companies.

2. PIONEER PATENTS MAY DISCOURAGE TECHNOLOGICAL ADVANCES, ESPECIALLY IN CUMULATIVE INDUSTRIES¹⁴⁵

Private property, including intellectual property, is essential to our way of life. . . . But reducing too much to private property can be bad medicine. Private land, for instance, is far more useful if separated from other private land by public streets, roads, and highways. Public parks, utility rights-of-way, and sewers reduce the amount of land in private hands, but vastly enhance the value of the property that remains. So too is it with intellectual property. Overprotecting intellectual property is as harmful as underprotecting it. Creativity is impossible without a rich public domain. . . . Culture, like science and technology, grows by accretion, each new creator building on the works of those who came earlier. Overprotection stifles the very creative forces it is supposed to nurture.¹⁴⁶

The very word “pioneer” suggests that a pioneering invention is much more valuable to society, or at least is a greater contribution to science and technology, than are subsequent additions, alterations, or “mere improvements” to the pioneer invention. Nevertheless, the patent system must not lose sight of the importance of improvement innovations. Rewarding pioneering inventors to the detriment of improvers is a

143. See *supra* note 142.

144. *Id.*

145. See generally Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research & the Patent Law*, 5 J. ECON. PERSP. 29 (1991); Rai, *supra* note 102; see also A.R. CHAPMAN, PERSPECTIVES ON GENETIC PATENTING: RELIGION, SCIENCE, & INDUSTRY IN DIALOGUE (1999).

146. Rebecca S. Eisenberg, *Technology Transfer & the Genome Project: Problems with Patenting Research Tools*, 5 RISK 163, 175 (1994) (quoting Judge Alex Kozinski in *Vanna White v. Samsung Elecs. Am., Inc.*, 989 F.2d 1512, 1513 (9th Cir. 1993) (dissenting)).

dangerous policy. It is important not to remove incentives that encourage subsequent researchers from contributing improvements. The theories of Kitch and Shumpeter overlooked the benefits of situations where more is gained from allowing other inventors to play a role in innovating and commercializing the pioneering invention.

First, these theories neglect the fact that all inventions, even pioneering ones, owe some acknowledgment to prior discoveries and inventions.¹⁴⁷ Second, although pioneer inventions may be technologically or creatively impressive, it may be the improvements that are commercially successful.¹⁴⁸ Third, patents may result in wasted resources. Competitors likely will expend time and money to “invent around” the patent claims. The contribution to society may merely be a redundant invention.¹⁴⁹ Fourth, while patents are important inducements to innovate, awarding broad property rights to a single firm may not be the best way to promote competition, which otherwise would increase the rate of innovation. As one economist found, “a market structure intermediate between monopoly and perfect competition would promote the highest rate of inventive activity.”¹⁵⁰ Thus, to speed up the pace of innovation, it may be important to provide some patent protection, but not extreme protection. Fifth, and perhaps most importantly, issuing patents to upstream, pioneering inventions in unpredictable, creative fields may stand in the way of progress because such unpredictable fields rely on the cumulative inputs and improvements contributed by other researchers.¹⁵¹ Because it is highly unlikely that a single patent holder will be

147. Inventing is a “continuous process . . . , in which the past is very much linked with the future . . . inventors built on the work of inventors who have come before.” Edmund W. Kitch, *Elementary & Persistent Errors in the Economic Analysis of Intellectual Property*, 53 VAND. L. REV. 1727, 1739 (2000).

148. “[I]mprovements in many cases dwarf the original work in terms of their practical significance.” Mark A. Lemley, *The Economics of Improvement in Intellectual Property Law*, 75 TEX. L. REV. 989, 997 (1997).

149. Ko, *supra* note 115, at 792-93.

150. MORTON I. KAMIEN & NANCY L. SCHWARTZ, MARKET STRUCTURE & INNOVATION 104 (1982). “[T]he optimal magnitude of the innovation will be the largest when the exogenous threat of entry is intermediate between no chance or rival entry and virtually certain rival entry.” *Id.* at 132 (citing R.R. DeBont, *Innovative Activity & Barriers to Entry*, EUROPEAN ECON. REV. 10, 95-109 (1977)). “[M]arket structure influences the speed with which transient quasi-rents are eroded away by imitators.” RICHARD R. NELSON & SIDNEY G. WINTER, AN EVOLUTIONARY THEORY OF ECONOMIC CHANGE 280 (1982).

151. Ko, *supra* note 115, at 792. “The argument for independence among researchers makes more sense if research leads down unexpected paths for which a course cannot be charted in advance, and if the success of research projects depends on insights and creativity that may differ from one investigator to the next.” Eisenberg, *supra* note 101, at 1066-67.

At their worst, [patents] can create obstacles to subsequent [research and development] and add to a thicket of rights that firms must negotiate their way past before they can get their products on the market. Patent protection is most likely to be an effective device for achieving technology transfer in the case of a patent that

suited ideally to identify future improvements, many diverse inventors should be encouraged to contribute to the development of the field.¹⁵² Such diversity is important because it is difficult to predict future uses of a pioneering technology, and even if such uses are predictable, the pioneering firm might not be the most competent at developing the technology.

The difficulty in expecting a single firm to control and direct innovation efficiently is likely even more prevalent in the biopharmaceutical field. It is true that in some industries coordination may be optimal. For example, in the field of computer electronics, it may be desirable for firms to coordinate to develop an industry standard such as a microprocessor on which many software companies can base their products. In contrast, the biopharmaceutical field is very different. Biomedical researchers do not develop standards so much as discover principles of nature and manipulate them for human use. While it may make sense for a single pharmaceutical firm to coordinate the development of a single compound for a single treatment of a disease, it would be better if multiple companies were involved if that compound has other uses, unanticipated by the first firm. Otherwise those uses will take longer to discover and develop.¹⁵³ In these circumstances, it is in society's best interest to allow many other firms the opportunity to seek out new uses for the compound. The benefits of efficient coordination for the development of one use are outweighed by the desire to avoid loss of other uses. Additionally, even if other firms do manage to find new uses, the transaction costs to license the invention from the patent holder must be low enough to encourage the other firms to develop the new uses.

This article does not argue that efficient or beneficial bargains

covers an end product for sale to consumers. It is least likely to be effective and most likely to interfere with subsequent research and product development in the case of a patent on a research tool that is to be used in subsequent stages of [research and development], but will not be incorporated into the end product as it is ultimately sold.

Eisenberg, *supra* note 146, at 168.

152. See Lemley, *supra* note 148, at 1049.

153. Golden, *supra* note 111, at 166-67.

The unpredictability of biotechnological development makes the coordination of subsequent invention implausible; allowing multiple firms to pursue a variety of commercial "spin-offs" seems a better strategy. Furthermore, because the granting of broad biotechnology patents tends to lead firms to engage in only "cosmetic differentiation," pioneer biotechnology patents appear unlikely to produce the kind of functional specialization that might create true "economics of coordination." Thus, in the context of modern biotechnology, any benefits from a "pioneer patent" are most probably outweighed by the costs of chilling invention and enabling licensing "hold-outs" that slow technological progress.

Id. (internal citations omitted).

never take place in the biopharmaceutical industry. Instead, it suggests that for optimal exploitation of an invention in the presence of a property right giving one firm market power, bargaining costs must be minimal. Indeed, under the ideal conditions assumed by Coasian theory,¹⁵⁴ issuing broad property rights to a pioneer is not a problem because a pioneer patent holder and an improvement patent holder (that is, the holders of "blocking patents") will bargain to an efficient outcome. Both parties have incentives to reach a deal as long as the improvement will increase the commercial success of the pioneer invention. In practice, however, such bargains may be difficult to achieve.¹⁵⁵ First, it may be difficult to value the inventive contributions made by the pioneer and subsequent inventors, especially in fields that require much development before commercialization.¹⁵⁶ Second, transaction costs could be high when a pioneer or improver has a false sense of the value of its contribution.¹⁵⁷ Third, a pioneer may simply fail to see how its invention may be improved.¹⁵⁸ Finally, there may be "irrational" reasons for the inability to strike a deal, such as "spite, pride, and anger."¹⁵⁹ Thus, the initial distribution of property rights can alter the bargaining parties' equilibrium level of output.¹⁶⁰ In such a situation, a court should intervene to promote a bargain.

A better solution would be to bestow on an early pioneer inventor only a narrow property right or no property right at all.¹⁶¹ Failures in licensing are especially dangerous when the patent protection in question covers a pioneering or upstream invention.¹⁶² This is because when transaction costs are too high, the incentive-to-innovate goals of the patent system break down. A patent is not meant to close off subsequent

154. See RONALD H. COASE, *THE FIRM, THE MARKET, & THE LAW* (1988); see also Ronald H. Coase, *The Problem of Social Cost*, 3 J. LAW & ECON. 1 (1960).

155. See Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 874 n.146 (1990).

156. Especially early in the development of a biopharmaceutical product "there is immense uncertainty over the technology's future development path and profitability," thus making it difficult to value innovations. Merges, *supra* note 135, at 75.

157. "[I]ndirect evidence suggests that the transfer of major improvements increases [transaction] costs." Ko, *supra* note 115, at 781.

158. See Merges, *supra* note 135, at 89.

159. *Id.* at 90.

160. Ko, *supra* note 115, at 781.

161. Because "efficient licensing will not always occur, intellectual property law must do more than determine that someone owns a particular intellectual property right: it must give some thought to who ought to own that right." Lemley, *supra* note 148, at 1061.

162. Such failures "will impede improvement in subsequent generations. The more absolute the property right given to original . . . inventors, the more critical efficient licensing is to subsequent innovation, and the more sensitive the industry is to market failures in licensing." *Id.* at 998-99.

innovation, but to reward an inventor for her investment. The licensing problem is amplified in the case of upstream patents.

What are the practical effects of patents in the biopharmaceutical industry? In general, a system has developed in which large, capital-intensive pharmaceutical companies coexist with small, capital-seeking biotechnology firms. The large companies clearly have marketing power, while the small firms may be subject to the whims of the capital markets.¹⁶³ Small companies depend on ownership of valuable patents for survival. However, broad patents are available to large pharmaceutical companies as well. The question is not whether broad patents are good for small biotechnology companies, but whether this system promotes frictionless Coasian bargaining. If so, the Coase theorem holds that it does not matter who gets the initial property right, or, by extension, how big it is. But since there is friction in practice, one should worry about who gets the initial property right and what happens after property rights are allocated.¹⁶⁴ For example, there could be holdup problems.¹⁶⁵ Eisenberg has provided empirical, if anecdotal, evidence for high transaction costs: “[p]rivate firms—both large, established pharmaceutical firms and small, young biotechnology companies—also report growing frustration with the administrative burden of renegotiating the terms of the agreements for the transfer of research tools and with attendant delays in research.”¹⁶⁶ She concluded that “initial allocations of intellectual property rights matter . . . because they either promote or retard the efficient dissemination of prior discoveries to

163. See generally Josh Lerner & Robert P. Merges, *The Control of Strategic Alliances: An Empirical Analysis of Biotechnology Collaborations*, Nat'l Bureau of Econ. Research, Working Paper No. 6014, 1997, (finding that the bargaining power of small biotechnology firms was dependent on their access to capital markets), available at <http://papers.nber.org/papers/w6014>.

164. See Robert P. Merges, *Institutions for Intellectual Property Transactions: The Case of Patent Pools*, in EXPANDING THE BOUNDARIES OF INTELLECTUAL PROPERTY: INNOVATION POLICY FOR THE KNOWLEDGE SOCIETY 123 (Rochelle Cooper Dreyfuss et al. eds., 2001); see also Josh Lerner, *The Patent System & Competition, Public Comment to the FTC & DOJ* (2002), available at <http://www.ftc.gov/opp/intellect/lernerjosh.pdf>.

165. Thus if property “rights are held by parties who will not undergo repeat interactions . . . [a] one-shot bargaining game results, where some party must assemble disparate rights to move forward with a valuable economic project. This is a setting ripe for holdups and bargaining breakdown, as the economic literature has long recognized.” Merges, *supra* note 164, at 128.

166. Eisenberg, *supra* note 117, at 225. Professor Eisenberg also notes that there seems to be a widely-shared perception that negotiations over the transfer of proprietary research tools present a considerable and growing obstacle to progress in biomedical research and product development. Scientists report having to wait months or even years to carry out experiments while their institutions attempt to renegotiate the terms of “Material Transfer Agreements,” . . . database access agreements, and patent license agreements. University technology transfer professionals report that agreements presented for the transfer of research tools impose increasingly onerous terms.

Id.

subsequent innovators.”¹⁶⁷

This transaction-cost problem is not only bad for the biopharmaceutical industry, but has social consequences as well.¹⁶⁸ An example is genetic tests. One study found that, due to fears of an infringement lawsuit, twenty-six percent of genetic testing labs stopped offering a test after a patent on the test issued.¹⁶⁹ Researchers believe the patents could reduce the quality of the genetic testing because the various labs will not be able to experiment with the testing and exchange data, and there will be fewer labs adding to the accumulation of knowledge.¹⁷⁰ Similarly, the presence of corporate relationships and ensuing patents has been cited as promoting an increased lack of sharing data and research products in academia.¹⁷¹ Interestingly, biopharmaceutical firms themselves have recognized these problems and have come up with a solution: they have attempted to preclude the possibility of obtaining some patents by freely dispensing some of their discoveries, thus creating patent-killing prior art.¹⁷²

Moreover, the problem could be exacerbated if there are multiple pioneer patent holders who hold overlapping property rights.¹⁷³ This problem has been termed the “tragedy of the anticommons,”¹⁷⁴ meaning that if a party must deal with multiple patent holders to develop a single invention, the probability of that innovation occurring is reduced. An

167. *Id.* at 226.

168. *Id.* at 233.

Even from the perspective of large, private firms, the value of foregone exchanges due to failed bargains over the transfer of research tools is often more than trivial. For example, a former scientist who now represents a major pharmaceutical firm in research tool negotiations indicated that, even when her firm is willing to pay \$20,000 for a license to a research tool, negotiations over contract language can take months or years, during which time the scientists often give up and turn their attention to something else.

Id. “A representative of another pharmaceutical firm explained that ‘the deal breaker [in negotiations over the transfer of research tools] typically isn’t cost, but terms and conditions.’ The terms and conditions that are so difficult to agree upon generally involve the allocation of speculative future value and risks.” *Id.*

169. Alison Motluk, *Scientists Hindered by Gene Patent*, 415 NATURE 577 (2002). The patent owner “wrote to labs offering to grant sublicenses for fees ranging from \$25,000 to \$250,000, plus royalties of \$20 per test.” *Id.*

170. This problem could cover testing for many genes such as those involved in hereditary hemochromatosis, Alzheimer’s Disease, breast cancer, and Fragile X syndrome. *Id.*

171. “[C]orporate involvement in academia has transformed from almost nothing two decades ago to a booming business today with, for example, Merck setting up a \$15 million deal with MIT that gives the company certain patent and licensing rights on joint discoveries over the next five years.” Nicholas Thompson, *Scientists Say Sharing of Key Data Has Slowed*, BOSTON GLOBE, Mar. 5, 2002, at C1.

172. This is especially true in the field of DNA sequencing. See Rai, *supra* note 102, at 825.

173. See Merges, *supra* note 164, at 128.

174. Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698, 698 (1998).

example is attempting to use the sequence of a gene in a therapy. If the PTO has issued patents for several fragments of that gene under its Expressed Sequence Tag (EST) policy,¹⁷⁵ then the developer of the therapy would have to bargain with each EST patent holder. One also can envision similar problems arising out of the hES cell patent. Because the technology is in such an early stage of development, it is likely that in an effort to put it to use, scientists will combine it with other technologies. If each of these technologies is covered by broad upstream patents, the innovator of the final product will have to bargain with each of those patent owners. Obviously, the upstream patent holders will be in a strong bargaining position. Additionally, it is likely that downstream innovators will be reluctant to develop uses because of the presence of the upstream patents unless bargains can be achieved *ex ante*.¹⁷⁶

3. PIONEER PATENTS MAY DISCOURAGE DEVELOPMENT OF THE SMALL BIOTECHNOLOGY FIRM MODEL¹⁷⁷

A wealth of small biotechnology firms sprouted in the San Francisco Bay Area (and ultimately internationally) after the founding of Genentech¹⁷⁸ in 1976. Biotechnology companies complement industry (agricultural and pharmaceutical) and academia by providing a third option for scientists to perform research and development, as well as a different vehicle for venture capital investment. The biotechnology industry is infused with the same entrepreneurial philosophy that helped create it.¹⁷⁹

Biotechnology companies operate using very different business models than those used by large pharmaceutical companies. Only a small fraction of biotechnology companies are likely to produce a mar-

175. See *infra* note 233.

176. Although the owners of the patent claim to deal with any problems through licensing, "three structural concerns caution against uncritical reliance on markets and norms to avoid a biomedical anticommons tragedy: the transaction costs of rearranging entitlements, heterogeneous interests of owners, and cognitive biases among researchers." Heller & Eisenberg, *supra* note 174, at 700.

177. See generally Jonathan M. Barnett, *Cultivating the Genetic Commons: Imperfect Patent Protection & the Network Model of Innovation*, 37 SAN DIEGO L. REV. 987 (2000); see also PETER S. COHAN, *THE TECHNOLOGY LEADERS: HOW AMERICAS' MOST PROFITABLE HIGH-TECH COMPANIES INNOVATE THEIR WAY TO SUCCESS* 73 (1997); D. Jane Bower & Erica Whittaker, *Client Communication & Innovative Efficiency in US & UK Biotechnology Companies*, in *NEW TECHNOLOGY-BASED FIRMS IN THE 1990s* 36, 40 (Ray Oakey ed., 1994).

178. See, e.g., Genentech Inc. fact sheet, http://www.gene.com/gene/25years/factsheet_biotech.html (last visited Nov. 16, 2002).

179. "In marked contrast with most research universities and pharmaceutical companies, biotechnology firms are mostly young, small, and privately held." Golden, *supra* note 111, at 117 (citations omitted).

ketable product within a reasonable time.¹⁸⁰ Instead, most biotechnology firms contribute innovative research tools,¹⁸¹ technology development, and cutting-edge ideas on possible future drug development to larger companies, or develop these innovations in joint ventures with larger companies.¹⁸² Instead of relying solely on large in-house corporate laboratories to perform basic research, large pharmaceutical companies increasingly have established partnerships with small firms and collaborations with universities,¹⁸³ due to their innovative creativity,¹⁸⁴ while small firms need resources contributed by large companies. In addition, large companies have struck deals with small biotechnology firms to spread risk.¹⁸⁵

This entrepreneurial collaborative system is more efficient at advancing the rate of discovery and development of biotechnology innovations, especially in unpredictable fields. "[T]raditional pharmaceutical companies, despite their superior innovative resources, lag far behind the small start-up companies in contributing to biotechnological innovations."¹⁸⁶ Although there are many possibilities, one explanation for the advantage of small firms is their lack of bureaucratic restraints.¹⁸⁷ Regardless of the explanation, it is clear that it is not in society's best interest to give any firm controlling status in unpredictable fields.

Some argue that small biotechnology companies are successful

180. *Id.*

181. "The evolving profit strategies of biotechnology firms often depend heavily on intellectual property rights in discoveries that are primarily inputs into further research. Eisenberg, *supra* note 117, at 227.

182. Frequently, their primary assets are knowledge, ideas, trained personnel, and patents. Before they develop a commercial product, they naturally seek financing through joint development projects with larger firms such as pharmaceutical companies, in which they trade intellectual property and technical expertise from cash and business savvy. The resulting cooperative structure of the biotechnology industry is well documented: in the mid-1990s, 81.8% of the United States biotechnology companies had a drug company research partner, 70.5% had a university research partner, 50% had a fellow biotechnology research partner, and 47.7% had a research institute research partner.

Golden, *supra* note 111, at 118-19 (citations omitted).

183. *Id.* at 122 (citations omitted). "Indeed, the biotechnology industry—dominated by small, young firms that rely for their continued existence on a complex network of collaborative research relationships—emerged in the 1990s as perhaps the leading exemplar of the cooperative approach to innovation through 'entrepreneurial science.'" *Id.* (citations omitted).

184. See Lerner & Merges, *supra* note 163; see also Barnett, *supra* note 177, at 1007.

185. Golden, *supra* note 111, at 122.

186. Ko, *supra* note 115, at 800.

187. See NELSON & WINTER, *supra* note 150, at 279. A large firm's "hierarchical structure and culture may be inimical to innovation, or at least inimical to radical innovation . . . [and] [i]nnovation incentives may . . . be weak in a large firm because it is difficult to design compensation schemes that accurately reflect responsibility for innovative inputs." Rai, *supra* note 102, at 825.

because they are protected by patents containing broad claims.¹⁸⁸ It is true that, in the short term, patent protection is desirable from the biotechnology company's perspective because it gives a small firm strong bargaining power. In the long term, though, the existence of broad, upstream patents held by other firms both discourages small companies from entering the research field and increases the burden on already existing firms, thus circling back to the problem of concentrating power in a few firms.¹⁸⁹ While a patent attorney will vigorously argue for the importance of broad patent protection for his firm, he will also complain about the existence of other patents¹⁹⁰: patents that siphon off money from the company via licenses or threatened litigation, or patents that may put the biotechnology company out of business. Such patent system-created "monopolies could distort the direction of research and eventually clog the 'small company' dynamism of the biotechnology industry itself, leading ultimately to its domination by giant companies with large concentrations of vested intellectual property rights, a situation that has arisen in the separate but related field of agricultural biotechnology."¹⁹¹

Thus, in practice, broad patent claims covering upstream or pioneering inventions do not always promote the flourishing of the biotechnology industry.¹⁹² Although a pioneer patent is surely valuable to a small biotechnology firm, such a patent may adversely affect other small firms. Additionally, there is nothing to stop a large pharmaceutical firm from obtaining such a patent and using it to the detriment of small firms. By concentrating power in a single entity, as described in Kitch's prospect theory, pioneer patents very well may be detrimental to the biotechnology industry.

188. Ko, *supra* note 115, at 800. Rather, the primary attraction of patents to biotechnology firms is placed elsewhere: "patent law facilitates innovation not so much by 'spurring' invention as by 'enabling' it, by providing small biotechnology firms, which are the heart of the American biotechnology industry, with an intermediate 'product'—patents—that they can use to attract investment." Golden, *supra* note 111, at 111.

189. See Barnett, *supra* note 177, at 1022.

190. See comments of Immunex Corporation's Vice President, Michael K. Kirschner, at FTC/DOJ hearings, Feb. 26, 2002, at <http://www.ftc.gov/opp/intellect/index.htm>.

191. Golden, *supra* note 111, at 172 (citations omitted). The "recent trend toward mergers and consolidation in human and animal biotechnology may be cause for incipient alarm." *Id.* There are currently about 1300 biotechnology firms. G. Steven McMillan et al., *An Analysis of the Critical Role of Public Science in Innovation: The Case of Biotechnology*, 29 RES. POL'Y 1, 2 (2000). See Antonio Regalado, *The Great Gene Grab*, Sept.-Oct. 2000, TECH. REV., at 48, 50. "[I]f in keeping with Kitch's theory, upstream patent rights are extremely broad, such that only a few vertically integrated firms exist, vertical integration considerably narrows the number of different research avenues that are likely to be pursued." Rai, *supra* note 102, at 835.

192. See Golden, *supra* note 111, at 167.

4. MANY BIOTECHNOLOGY PIONEER INVENTIONS LIKELY WOULD
HAVE BEEN DISCOVERED IN THE ABSENCE OF PATENT
LAW'S INCENTIVES

The patent system is designed to provide incentives to inventors to make investments of time and money worthwhile. In a very real sense, then, inventions that would exist in the absence of the patent system should not be covered by patent protection. In this regard, a distinction can be made between upstream and downstream research. Upstream, basic research may occur in the absence of patents, especially if it is already occurring in academic laboratories. Indeed, federal funding, not the patent system, generally provides the incentive in such situations. In contrast, improvement research, much of which is aimed at commercialization of the pioneering invention, likely requires patent incentives. Many academic laboratories are not interested in completing the details of an invention for commercialization purposes. Instead, they are interested in uncovering novel principles and discoveries of science and technology. This provides another reason to take care in issuing patents covering upstream, pioneering inventions. Private firms, which generally commercialize upstream discoveries with downstream improvements, must not be impeded by pioneer patents covering the upstream discoveries.

For example, academic scientists, who have driven the revolutionary advances in biomedical science, are not generally motivated by the possibility of obtaining patents. Instead, they seek publication and the esteem of their peers.¹⁹³ Indeed, much biotechnology upstream, basic research would take place in the absence of the patent system.¹⁹⁴ This is probably true for many pioneering inventions and certainly would have been true for hES cells (in the absence of the government's reluctance to fund this research), whose existence has been known for a long time.¹⁹⁵ Scientists have been struggling for decades to isolate other types of stem cells, such as adult blood and neural stem cells.¹⁹⁶ Nevertheless, patent

193. See Rebecca S. Eisenberg, *Proprietary Rights and the Norms of Science in Biotechnology Research*, 97 YALE L.J. 177, 182 (1987); Robert K. Merton, *The Normative Structure of Science*, in THE SOCIOLOGY OF SCIENCE 270 (1973); Arti K. Rai, *Regulating Scientific Research: Intellectual Property Rights and the Norms of Science*, 94 NW. U. L. REV. 77 (1999).

194. See *Kewanee Oil Co. v. Bicron Corp.*, 416 U.S. 470 (1974).

The ripeness-of-time concept of invention, developed from the study of the many independent multiple discoveries in history, predicts that if a particular individual had not made a particular discovery others would have, and in probably a relatively short period of time. If something is to be discovered at all, very likely it will be discovered by more than one person.

Id. at 490 (citations omitted).

195. *Stem Cells: Potential for Good?*, *supra* note 17.

196. See Ruthann Richter, *Stem Cell Pursuits*, 19 STAN. MED. 11 (2002).

protection likely is a motivating factor for many inventors of improvements. For example, academic laboratories are not going to spend the time and money to guide a therapy through Food and Drug Administration (FDA) trials.

It thus seems important to distinguish between the two types of inventions before a patent is awarded. Because of the difficulty in determining what is an upstream or pioneer invention, however, a better solution may be to issue patents whose claims are coextensive in scope with the invention, that is, a narrow patent.¹⁹⁷ If this model had been applied to the hES cell patent applications, WARF would have ended up with patent protection covering the method of culturing the hES cells, and product claims to the unique cell-lines made by Dr. Thomson. WARF would not own claims to all freshly purified hES cells.

III. A SOLUTION TO THE PROBLEM CREATED BY THE ISSUANCE OF THE hES CELL PATENT PRODUCT CLAIMS

How can the market distortions created by the overly broad ES cell patents (and exacerbated by President Bush's decision) be ameliorated? I propose that the best solution is to turn to existing patent doctrines to assess the validity of the WARF patents.¹⁹⁸ Additionally, in the future this general analysis should be more strictly applied to other types of upstream inventions. In a general sense, because the costs of misallocation of a property right could be large, there should be a presumption against the issuance of broad, upstream, pioneer-type patents, especially those covering purifications of products of nature. While the patent system is not legally in a position to distinguish between pioneer and improvement inventions as long as both rise above the patentability threshold,¹⁹⁹ the scope of the patent can be tailored during prosecution of the patent or afterward during litigation. Moreover, such claims (as the hES cell patent product claims) may be invalidated by the courts²⁰⁰ if

197. "Although basic research conducted in universities can never completely substitute for industrial inventions, narrowing patent scope for biotechnology makes sense, because alternatives to financial reward may be sufficient to stimulate inventions." Ko, *supra* note 115, at 794. Also note the "technological resignation" view: "although the patent system indeed has an impact upon the progress of individual inventions, the advance of technology is an inevitable societal force in which the scheme of patents can play only a marginal role." Thomas, *supra* note 131, at 39.

198. Congress might also consider the possibility of invalidating the patent or requiring compulsory licensing in view of the implications of President Bush's decision. In the absence of federal funding, we must be especially careful how we allocate property rights to these technologies. See *infra* note 205.

199. "It is not enough to say that intellectual property law favors 'creators'—for here we have creators on both sides of the equation, and the law must choose between them." Lemley, *supra* note 148, at 998.

200. See *infra* Part III.A. (discussing several grounds of invalidation).

they survive the PTO's examination process and their scope cannot be narrowed.

The courts and the PTO should pay closer attention to maintaining strict standards of patentability for upstream or pioneering inventions. The patent system has guided the assessment of the patentability of upstream research in prior, similar situations. For example, in recognizing that "overprotection of algorithms may stifle innovation by raising the costs of subsequent innovation,"²⁰¹ the PTO clarified its position on patenting software in a statement of guidelines, which states that "mathematical algorithms are, as such, unpatentable, but that applications of such algorithms may be protectible as new processes."²⁰² The PTO responded similarly to a recent perceived crisis concerning patents of DNA sequences.²⁰³ The PTO should demonstrate the same concern to the case of the ES cell patents and future applications for claims to freshly purified cells. Federal funding, not the patent system, should provide the incentives for uncovering these upstream discoveries. But regardless of federal funding, the patent system should not provide overly broad property rights to them.

If patent protection is too broad, there are two possible ways of dealing with this problem through a shift in patentability doctrine at the level of patent prosecution. First, the requirements of patentability, such as new invention, utility, enablement, and written description, could be more rigorously applied by the PTO. Second, new categorical rules could be developed, proscribing the patenting of certain types of substances; in this case, cells removed from a human body. The courts could also develop these standards in patent litigation by invalidating claims that do not strictly adhere to the patent doctrines. In contrast to such a doctrinal shift, the courts could construe the claims' scope narrowly through litigation.²⁰⁴ Additionally, the courts could more readily allow infringement of such claims. For example, the reverse doctrine of equivalents may be applied to excuse infringement by improvement inventions.²⁰⁵

201. Stanley M. Besen & Leo J. Raskind, *An Introduction to the Law and Economics of Intellectual Property*, 5 J. ECON. PERSP. 3, 9-10 (1991). The PTO's new guidelines were prompted by "[r]eports in 1988 and 1989 that the [PTO] had adopted a more liberal approach to software patent applications, which might result in granting patent protection to fundamental building blocks of research." *Id.*

202. *Id.*

203. Rebecca S. Eisenberg, *Analyze This: A Law and Economics Agenda for the Patent System*, 53 VAND. L. REV. 2081, 2086-87 (2000).

204. Golden, *supra* note 111, at 108. Note, though, that the solution of allowing courts to decide the scope of claims promotes the problem of introducing expensive ambiguity into the system by allowing the PTO to approve broad claims, leaving the courts to clarify and invalidate.

205. Additionally, although outside the scope of this paper, a compulsory licensing scheme

In a more specific sense, all of these approaches could be applied to the hES cell problem. First, should hES cells be patentable? I propose that hES cells (as distinct from hES cell-lines) should not be patentable. However, any narrowly defined, downstream therapies coming out of this research may be patented. For example, patent protection would be available for individual hES cell-lines developed as described in the patent specification,²⁰⁶ and for the method of isolation of hES cells. In the short term, a strong case could be made for the revocation of WARF's ES cell patent product claims. The PTO could reexamine the issued patent, checking the examination procedure for mistakes.²⁰⁷ Under limited conditions,²⁰⁸ if the PTO agreed with this argument and found that the ES cell patent product claims were mistakenly issued, it could revoke the claims. Second, if the product claims are not revoked, courts can invalidate them in infringement litigation. Third, if the product claims are not invalidated, their scope could be narrowly construed to cover only the cell-lines described in the specification. Finally, the courts or Congress could make clear that such vaguely defined cell isolations are not patentable. The remainder of this Part discusses the doctrinal bases on which the PTO or courts may solve this problem.

*A. Invalidating the WARF hES Cell Patent Product Claims on
Grounds that Traditional Patentability Requirements Were
Not Satisfied*

A solution to the problem of disproportionate control of hES cell research by WARF is the invalidation of the WARF patent product claims. Of course this would require a willing litigant and many years

could be applied to broad, upstream patented inventions. Yet, there are many problems with such a solution, not the least of which would be the setting of a dangerous precedent. "The primary argument against compulsory licensing is that it allows courts, not the parties themselves, to set the terms of exchange." *Merges, supra* note 135, at 99. Alternatively, as part of its deliberations on President Bush's hES cell decision, Congress could specify that the product claims are unenforceable in light of President Bush's decision. This would excuse the courts from having to make the decision. It may be more desirable to do it this way because it could be a number of years before a case reaches the courts. Also, companies might not invest in hES cell improvement research for fear of losing a court battle. Additionally, uncertainty in how a court might interpret the scope of the ES cell patents will likely make bargaining inefficient. And, if through these solutions patent law is unable to "achieve the ideal balance between the incentives for invention and dissemination, . . . perhaps Congress [should] provide biotechnology with a special regime of protection." *Golden, supra* note 111, at 108.

206. Thus, individual hES cell-lines would be protectable, just as cell-lines were found patentable in *Moore v. Regents of the University of California*, 793 P.2d 479, 271 (Cal. 1990). See *infra* Part III.A.3 (discussing *Moore*).

207. 35 U.S.C. §§ 301-307 (2002); 37 C.F.R. §§ 1.510-1.570 (2002).

208. See Allan M. Soobert, *Breaking New Grounds in Administrative Revocation of U.S. Patents: A Proposition for Opposition—and Beyond*, 14 SANTA CLARA COMPUTER & HIGH TECH. L.J. 63 (1998).

before final resolution. Some avenues of attack are laid out below. Several patent doctrines protect basic and upstream research (as opposed to downstream applications of it) from being declared off-limits by the issuance of a patent. These doctrines include the utility, enablement, and written description requirements as well as the prohibition on patenting products of nature.

1. ARE ES CELLS PATENTABLE SUBJECT MATTER?

a. *The Product-of-Nature Prohibition on Patentability*

A patentable invention must be new.²⁰⁹ Products of nature are theoretically unpatentable because they are not new, even if they were previously unknown to humans. Moreover, a product of nature is hardly an invention. As stated by the Supreme Court in applying this doctrine to cells, "the relevant distinction [is] not between living and inanimate things, but between products of nature, whether living or not, and human-made inventions."²¹⁰ Thus, while a genetically modified cell is patentable, the Supreme Court did not hold that *any* cell is patentable. This prohibition also serves to ensure that items that may be relied on by people cannot be removed from general use by the issuance of a patent. For example, one cannot patent a gene that exists inside a person, thus requiring living people to pay royalties for the "use" of that gene. The product-of-nature prohibition would thus seem to strongly block the patenting of hES cells. However, the patent system has allowed an exception to the doctrine: purified products of nature may in some cases be patentable.

209. "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title." 35 U.S.C. § 101 (2002); *see also id.* § 102.

210. *Diamond v. Chakrabarty*, 447 U.S. 303 (1980), established the validity of patents on "life." In that case, the invention in question was a bacterium containing artificially introduced plasmids. The patent examiner rejected the product claims covering the bacterium on "two grounds: (1) that micro-organisms are 'products of nature,' and (2) that as living things they are not patentable subject matter under 35 U.S.C. § 101." *Id.* at 306. Five Supreme Court Justices thought otherwise, finding that the "claim is not to a hitherto unknown natural phenomenon, but to a nonnaturally occurring manufacture or composition of matter—a product of human ingenuity 'having a distinctive name, character [and] use.'" *Id.* at 309-10. This genetically modified organism could be thought of as an "invention," because it truly had not existed before. Thus, it is distinct from patenting a preexisting purified or isolated cell, for example an ES cell. The "Supreme Court did not reach the issue of whether naturally-occurring microorganisms that have been newly isolated or purified also fall within the ambit of 'manufactures' or 'compositions of matter.'" Eisenberg, *supra* note 193, at 189.

b. *The Purification Exception to the Product-of-Nature Patentability Prohibition*

Is *purified* biological matter simply a discovery of a product of nature, or is it a human-made invention? The Court of Customs and Patent Appeals²¹¹ found the argument that purifications are unpatentable under section 101 “wholly lacking in merit. The biologically pure culture of [the claim] clearly does not exist in, is not found in, and is not a product of, ‘nature.’ It is man-made and can be produced only under carefully controlled laboratory conditions.”²¹² The question is not so simply answered though. Referring to patents covering DNA sequences, Justice Stephen Breyer stated:

The most difficult question is deciding when these or other products of genetic research reflect only discovery of an existing aspect of nature, like Einstein’s discovery of the principles of relativity, and when they amount to a protectable invention or useful device. Should it matter if the more apt description of the scientists work is the discovery of how a portion of the body functions, rather than the invention of how to use a part of that body to perform a useful, say, diagnostic, task? This latter question will sometimes seem unanswerable. Cloning a previously unknown DNA sequence is a little like the “discovery” of a preexisting part of the human body; it is also something like the expensive, time-consuming, and novel isolation of a previously unknown molecule.²¹³

There is some tension here that probably emanates from the difficulty in characterizing biotechnology innovations.²¹⁴ Patents originally were envisioned to cover inventions such as machines, things clearly that had not previously existed. But many biological discoveries have existed previously. It is worth noting that patents on machines did not provide protection equivalent to that provided by the WARF product claims because other machines that could carry out the same function might be invented, escaping the patent claims. In contrast, there is only one chemical or biological structure. There is no way around the WARF product claims. One cannot invent a new type of freshly purified hES cell.

The courts may be willing to overlook the product-of-nature prohi-

211. The predecessor to the U.S. Court of Appeals for the Federal Circuit.

212. *In re Bergy*, 563 F.2d 1031, 1035 (C.C.P.A. 1977).

213. Stephen G. Breyer, *Genetic Advances and Legal Institutions*, 28 SYMP. J.L. MED. & ETHICS 23, 27 (2000).

214. Further complicating the issue, courts have held that purified naturally occurring *metals* are *not* patentable subject matter. *See, e.g.*, *Gen. Elec. Co. v. DeForest Radio Co.*, 28 F.2d 641 (3d Cir. 1928). In the current pro-patent environment, however, it is questionable whether courts would uphold these old cases. ROBERT P. MERGES & JOHN F. DUFFY, *PATENT LAW AND POLICY: CASES AND MATERIALS* (3d ed. 2002).

bition when purification or isolation is both difficult and useful. In such a case, the purification is a large inventive leap. For example, Judge Learned Hand espoused such an economic argument in *Parke-Davis & Co. v. H.K. Mulford Co.*,²¹⁵ where he upheld claims to purified adrenaline because they “became for every practical purpose a new thing commercially and therapeutically.”²¹⁶ Before the purification of adrenaline, people settled for a much less potent and less safe form of adrenaline. The purification was an important step in the progress of innovation. Thus, at least regarding chemical and biotechnology discoveries, it may be true that the product-of-nature doctrine is no longer an important bar to patentability. This is true because many biopharmaceutical inventions require purifying chemical or biological materials to purity levels considered unnatural according to Judge Hand’s formulation. Note, however, that this formulation does not apply to the hES cell patent product claims.

c. *hES Cells in Particular*

The PTO obviously has viewed purified ES cells as patentable subject matter.²¹⁷ At present, the issue has not appeared before courts. While patent infringement litigation involving adult bone marrow-derived stem cells has been heard by the Federal Circuit, the issue of whether the claim covered patentable subject matter²¹⁸ was never reached.²¹⁹ Instead, the court focused on determining what was meant by the language “substantially free” when describing purification of the blood stem cells, and determining whether the claims were infringed. Because the claim²²⁰ was very similar to the WARF patent and the court did not feel compelled to address its patentability with respect to the product-of-nature prohibition, it seems unlikely that courts will overturn the PTO’s decision to grant a patent for ES cells.

But the courts should look more deeply into the purification exception in this context. Analysis of the hES cell patents reveals that the purification exception to the product-of-nature prohibition has been abused. First, the patented hES cells are not purified in the sense that the adrenaline was in *Parke Davis*. In that case, the inventive step was

215. 189 F. 95 (C.C.S.D.N.Y. 1911).

216. *Id.* at 103.

217. Todd Dickinson, Acting Assistant Secretary of Commerce and Acting Commissioner of Patents and Trademarks, comments before the Subcommittee on Labor, Health and Human Services, Education and Related Agencies of the Senate Appropriations Committee, Jan. 12, 1999, available at <http://www.uspto.gov/web/offices/ac/ahrpa/opa/bulletin/stemcell.pdf>.

218. 35 U.S.C. § 101 (2002).

219. *Johns Hopkins Univ. v. CellPro, Inc.*, 152 F.3d 1342 (Fed. Cir. 1998).

220. See U.S. Pat. No. 4,714,680 (issued Dec. 22, 1987).

preparing adrenaline in such a way that impurities were removed. In the hES cell patents, purification per se is not the inventive step. It is trivial to separate hES cells from the blastocyst. Instead, the inventive step was developing a method to keep them alive in culture in their pluri potent state. It is this method that should be patented, not the "purified" hES cells themselves. Second, Judge Hand's holding in *Parke Davis* was likely motivated by economic considerations: by removing the impurities, the adrenaline immediately became a commercially viable and much sought-after product. The inventive step directly led to a commercial use. In contrast, as described in the hES cell patents, the separation of hES cells from the blastocyst added no economic value to the technology. First, such separation was easily performed prior to Dr. Thomson's work. Second, the disclosed technology is very far removed from commercialization. It might be useful to keep in mind the Supreme Court's comments in *Brenner v. Manson* that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. '[A] patent system must be related to the world of commerce rather than to the realm of philosophy'"²²¹

The courts and the PTO should reinvigorate the product-of-nature prohibition, and overlook it only in cases where purification truly represents a human inventive step that leads directly to commercialization (that is, a downstream invention). Along with prohibition on patenting formulas and natural laws, the product-of-nature prohibition serves a useful function: it permits free exchange of upstream information upon which many improvers rely to develop useful innovations. In a real sense, such upstream research is a stem, just like stem cells, from which many varied innovations may be developed. Additionally, the product-of-nature prohibition should also be more rigorously applied to other biopharmaceutical patent applications.

2. THE UTILITY REQUIREMENT

The utility requirement²²² for patentability encompasses requirements of usefulness in the invention as well as disclosure of that usefulness in the patent specification.²²³ In that sense it is tied together with the enablement and written description requirements discussed in the next section. To satisfy the utility requirement the patent applicant must disclose a specific, practical use for the claimed invention and disclose

221. *Brenner v. Manson*, 383 U.S. 519 (1966).

222. The utility requirement is found in 35 U.S.C. § 101: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title."

223. Eisenberg, *supra* note 203, at 2086-87.

the best mode of using the invention such that those having ordinary skill in the art can make and use the invention without having to do undue experimentation.²²⁴ A "prophetic," that is, not yet tested or operable, disclosed use "may be sufficient if there is no reason to doubt that the instructions are adequate to make the invention operable for the described use without undue experimentation."²²⁵ The utility requirement may sometimes be problematic in the sense that only a single use need be demonstrated; when a patent is granted on the basis of one use, the patent rights extend to all possible uses.²²⁶ Thus, it is especially important that the PTO and the courts strictly require an adequate use before passing on the utility of the invention.

What constitutes an adequate use? The utility requirement can be conceptualized as a timing device: an invention is simply not ready for patent protection if there is no demonstrated practical use. Thus, the utility requirement may be a good way to distinguish upstream from downstream research.²²⁷ The Supreme Court recognized this problem in *Brenner v. Manson*, in which it stated that if a patent were allowed prior to showing utility, it "may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development, without compensating benefit to the public."²²⁸ Yet, how is use defined in biotechnology patents? Clearly a drug that has passed FDA approval is a downstream product. Nonetheless, as stated above, many upstream biotechnology discoveries are also useful. For example, upstream techniques or chemicals used to develop the drug might be sold as final product research tools. Conversely, a compound that might serve as a downstream drug may also be used as a research tool.

Additionally, usefulness has not been defined by the courts as being coextensive with marketability. Recent Federal Circuit cases suggest the utility requirement is not much of an impediment to patentability. Biotechnology inventions have been held useful even with the concession that much future research and development is needed prior to putting the invention on the market.²²⁹ For example, in *In re Brana*,²³⁰ claims to novel compounds that are structurally similar to other compounds that

224. See 35 U.S.C. § 112 (2002); *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988); Eisenberg, *supra* note 193, at 207-08.

225. Rebecca S. Eisenberg & Robert P. Merges, *Opinion Letter as to the Patentability of Certain Inventions Associated with the Identification of Partial cDNA Sequences*, 23 A.I.P.L.A. Q. J. 1, 16 (1995). See *In re Strahilevitz*, 668 F.2d 1229 (C.C.P.A. 1982).

226. Eisenberg & Merges, *supra* note 225, at 14.

227. Rai, *supra* note 102, at 839.

228. *Brenner v. Manson*, 383 U.S. 519, 534 (1966).

229. Eisenberg, *supra* note 203, at 2087.

230. 51 F.3d 1560, 1567 (Fed. Cir. 1995).

displayed antitumor activity in mice were rejected by the PTO because they were not independently shown to be effective in humans. The Federal Circuit reversed. The impetus for the reversal likely rests in the difficulties of invention in the biotechnology industry. There are many potential pharmaceutical compounds that could be used to treat diseases. Such compounds usually take years to develop and years of rigorous testing to satisfy the FDA's requirements of safety and effectiveness. The court did not believe that the patent system should require the same rigorous evidence of safe and efficacious treatment of disease as evidence of usefulness: "Were we to require Phase II testing in order to prove utility, the associated costs would prevent many companies from obtaining patent protection on promising new inventions, thereby eliminating an incentive to pursue, through research and development, potential cures in many crucial areas such as the treatment of cancer."²³¹

Although the utility requirement may be easily satisfied according to the courts,²³² in the context of DNA sequence patents—and now in the hES cell patents—the utility requirement could do some work. For example, just as for hES cells, patentability of DNA sequences is problematic. WARF claims to have a stake in all future hES cell-lines. Similarly, simply by sequencing a DNA sequence, a DNA sequence patent holder could claim partial rights to any therapy developed either using or acting on the DNA sequence. It is also likely that, because there are a finite number of genes, such DNA patents will end up being relevant to many therapeutic discoveries. In response to such concerns, the PTO established new utility examination guidelines for consideration when evaluating patent claims comprising DNA sequences.²³³

The guidelines now require *specific and substantial* utility.

This contrasts with a *general* utility that would be applicable to the broad class of the invention. For example, a claim to a polynucleotide whose use is disclosed simply as a "gene probe" or "chromosome marker" would not be considered to be *specific* in the absence of a disclosure of a specific DNA target. Similarly, a general statement of diagnostic utility, such as diagnosing an unspecified disease, would ordinarily be insufficient absent a disclosure of what conditions can be diagnosed.²³⁴

Substantial utility is a "utility that defines a 'real world' use. Utili-

231. *Id.* at 1568.

232. Eisenberg, *supra* note 203, at 2085.

233. Revised Interim Utility Guidelines Training Materials, at www.uspto.gov/web/menu/utility.pdf [hereinafter Training Materials]. It must be noted that the courts are not bound to these PTO Guidelines. See *Merck & Co. v. Kessler*, 80 F.3d 1543, 1549-50 (Fed. Cir. 1996); see also Utility Examination Guidelines, 66 Fed. Reg. 1092 (2001).

234. Training Materials, *supra* note 233, at 5-6.

ties that require or constitute carrying out further research to identify or reasonably confirm a 'real world' context of use are not substantial utilities."²³⁵ Some examples of insubstantial utilities given by the PTO include "[b]asic research such as studying the properties or the claimed product itself or the mechanisms in which the material is involved . . . [and a] method of treating an unspecified disease or condition."²³⁶ Thus, it is not enough simply to isolate and list a new DNA sequence and describe further research that is needed to develop a real-world use. One must now demonstrate a clear use for it. The PTO and the courts should require the same demonstration of use when reviewing patents covering any freshly purified cells, especially those derived from humans.

These recent developments concerning DNA sequences suggest that WARF's hES cell patent product claims should have been rejected based on lack of utility, at least with regard to therapeutic uses. No therapy has yet been developed, or even begun to be developed. The only use demonstrated by Dr. Thomson was a research use. Thus, it is very much like the "bare genetic sequence" deemed unpatentable under the new PTO guidelines. This is not to say that research uses are not adequate for satisfying the utility requirement, but a real-world research use, other than merely studying the cells themselves, must be clearly demonstrated. To analogize to DNA patents, claiming stem cells for research use would be more like claiming DNA in general (in contrast to individual DNA sequences) for research use. If this is the standard of utility, anything could be claimed for research use. Yet, as described above, the PTO requires more of a showing of utility for DNA patents. One must now show some specific understanding of the importance of the specific sequence and how it might be used in a narrow sense. Similarly, hES cells are likely to have varied and distinct properties depending on from whom they are derived, how they are derived, and how they are treated in culture. The courts and the PTO should require a more detailed showing of utility of each individual hES cell-line based on its unique properties. By strictly construing the utility requirement in this way, the PTO and the courts can prevent overbroad patenting of ill-understood upstream research. A reasonable implication of such a policy would be that only unique individual cell-lines for which a clear use has been shown may be patentable. For example, perhaps one inventor may discover an hES cell-line that is particularly good at fighting liver cancer, while another may derive a different hES cell-line that is more suitable for treating Parkinson's Disease.

235. *Id.* at 6.

236. *Id.*

3. ENABLEMENT AND WRITTEN DESCRIPTION: COMPARISON OF
FRESHLY PURIFIED hES CELLS TO HUMAN-MADE
hES CELL-LINES

The enablement requirement specifies that the invention must be disclosed in such detail that others can make and use it without having to perform undue experimentation.²³⁷ The written description requirement serves to announce to the public what the invention is and to put the public in possession of it: the invention must be described in "sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention . . . with all of its limitations."²³⁸ While these two requirements are doctrinally distinct, they can be discussed together for the purposes of this article. Both emanate from the bargain the patent system makes with the inventor: a limited monopoly in exchange for disclosure. If an invention has not been enabled or adequately described in writing²³⁹ the PTO should not issue the patent, and if it does issue it, the courts should invalidate the relevant claims.

Additionally, these doctrines may be the most appropriate patent doctrines for defining claim scope.²⁴⁰ Both doctrines aim to ensure that the inventor was in possession of the claimed invention. The goal is to ensure that the scope of the claims is not broader than the invention possessed and disclosed.²⁴¹ These doctrines thus attempt to limit the

237. *In re Wands*, 858 F.2d 731, 735 (Fed. Cir. 1988); *see also* *Consol. Elec. Light Co. v. McKeesport Light Co.*, 159 U.S. 465 (1895) (finding that description of a single fiber did not entitle the patentee to a monopoly for all fibrous materials for incandescent conductors).

238. 66 Fed. Reg. 1099, 1104 (Jan. 5, 2001); *see also* *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555 (Fed. Cir. 1991). There is an exception, however: later discovery of divergent properties of species within the genus will not result in invalidation of the claims.

[E]nablement is tested only as of the time the original inventor files for a patent. If the original inventor has *at that time* enabled the use of an entire class of products, a claim covering that entire class is warranted. But if the class *subsequently* expands to include other species not conceived at the time of the first patent, the generic claim language will allow the first inventor to capture those new species within the scope of his claim.

Lemley, *supra* note 148, at 1009.

239. These doctrines arise from 35 U.S.C. § 112 (2002).

240. *See* *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997); *see also* *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200 (Fed. Cir. 1991); *infra* Part III.B.2.

241. As the Supreme Court explained,

[T]o hold that one, who had discovered that a certain fibrous or textile material answered the required purpose, should obtain the right to exclude everybody from the whole domain of fibrous and textile materials, and thereby shut out any further efforts to discover a better specimen of that class than the patentee had employed, would be an unwarranted extension of his monopoly, and operate rather to discourage than to promote invention.

Consol. Elec. Light Co., 159 U.S. at 476.

claims to the inventive step, without narrowing the claims to the point where the patent becomes worthless.²⁴² Another useful function of these requirements is that they force the patentee to clearly define the invention, in theory permitting others to know clearly the boundaries of the invention in order to avoid infringing it.

Problems of appropriately defining claim scope arise when a patentee claims a genus in an *unpredictable* field such as biotechnology.²⁴³ Patentees who claim a genus usually only describe a few species within the genus. In such claims, the specification must describe "a representative number of species"²⁴⁴ that must be "representative of the entire genus."²⁴⁵ But the written description requirement is not satisfied when an essential feature of the invention is not disclosed.²⁴⁶ This is particularly problematic in unpredictable fields in which not much is known about the genus: "adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species with the genus."²⁴⁷ Broad claims may be rejected on the basis of too few demonstrated examples.

The enablement and written description requirements have been used to invalidate or narrow the scope of broad claims in biotechnology patents. For example, in *Amgen, Inc. v. Chugai Pharmaceutical*,²⁴⁸ the Federal Circuit found that a claim directed toward all DNA sequences

242. "The boundary defining the excludable subject matter must be carefully set: it must protect the inventor, so that commercial development is encouraged; but the claims must be commensurate with the inventor's contribution. Thus the specification must meet the requirements of § 112." *In re Wands*, 858 F.2d at 741.

243. "In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970). "The scope of the claims must be less than or equal to the scope of the enablement." *Nat'l Recovery Tech., Inc. v. Magnetic Separation Sys., Inc.*, 166 F.3d 1190, 1196 (Fed. Cir. 1999). *See also In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). But, "where a number of materials or devices are substitutable because they have similar characteristics, the patentee may claim the generic class of materials, so long as he describes the general class and its characteristics with sufficient precision that others can identify and use them without 'undue experimentation.'" Lemley, *supra* note 148, at 1003.

244. 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001).

245. *Id.*

246. This principle goes back to *Consolidated Electric Light Co.*, 159 U.S. 465 (1895). In that case, a claim to the use of any vegetable fiber (that is, an entire class of products) as a filament in a lamp was not upheld because the inventors "had not done sufficient work to justify treating all vegetable fibers as interchangeable." Lemley, *supra* note 148, at 1002. The Supreme Court ties the concept to the inventive step: "[I]f . . . there were some general quality, running through the whole fibrous and textile kingdom, which distinguished it from every other, and gave it a peculiar fitness for the particular purpose, the man who discovered such a quality might justly be entitled to a patent . . ." *Consol. Elec. Light Co.*, 159 U.S. at 475. The hES cell patents should be found invalid under *Consolidated Electric Light Co.* reasoning.

247. 66 Fed. Reg. 1099, 1106 (Jan. 5, 2001).

248. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1214 (Fed. Cir. 1991).

that will encode any polypeptide having the blood-cell-production-increase activity of erythropoietin (EPO) was too broad. According to the court this claim was not enabled because it "is not sufficient, having made the gene and a handful of analogs whose activity has not been clearly ascertained, to claim all possible genetic sequences that have EPO-like activity."²⁴⁹ Similarly, the Federal Circuit has also found non-enabled a claim to a method for producing any peptide in any plant cell because it was supported only by a single example.²⁵⁰ The court found that there was too much unpredictable research remaining in order to produce any peptide in any cell.²⁵¹ These are examples of genus claims that were not sufficiently enabled by description of species.

Additionally, even if a genus is enabled, it may not pass the written description requirement. The Federal Circuit has invalidated on written description grounds a claim to the complementary DNA encoding human insulin because the specification only disclosed the sequence of rat insulin and then described how one might isolate the human version. An adequate written description of the human insulin sequence was not provided.²⁵² In the case of gene patents, a "definition by function . . . does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is."²⁵³

Comparing the WARF hES cell patent product claims to the courts' and PTO's approach to DNA sequence patents indicates that the WARF product claims do not satisfy the written description or enablement requirements. For example, the PTO has stated that a "biomolecule sequence described only by a functional characteristic without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for

249. *Id.*

250. *In re Goodman*, 11 F.3d 1046, 1052 (Fed. Cir. 1993).

251. *Id.* "For instance, production of peptides in monocotyledonous plants involves extensive problems unaddressed by [the] specification." *Id.*

252. *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997).

253. *Id.*; see also Mark J. Stewart, *The Written Description Requirement of 35 U.S.C. § 112(1): The Standard after Regents of the University of California v. Eli Lilly & Co.*, 32 IND. L. REV. 537 (1999).

[I]t would seem that the holding in *Lilly* . . . avoided a disaster that would have crippled the biotechnology industry. . . . Through application of the written description requirement, courts can distinguish between claims to technologies that are too broad or basic to justify patent protection, and those dealing with other types of technologies that are more predictable and may justify broader protection. Thus, the Federal Circuit has decided that the uniqueness of biotechnology inventions claiming DNA sequences requires the application of a stringent written description requirement to protect the public from inventors seeking to slow the pace or research by preempting future developments before they arrive.

Id. at 563-64.

written description purposes, even when accompanied by a method of obtaining the claimed sequence.”²⁵⁴ This directly applies to the hES cell patent product claims. The cells in the claims are described by functional characteristics (for example, their ability to stay alive in culture without differentiating, and then to differentiate into many types of cells). There is no known correlation between that function and the scientific basis for it. This is a problem because different ES cells may behave differently. ES cells are likely to be functionally distinct depending on how and from where they are isolated, and how they are maintained.

The hES cell claims are also analogous to those at issue in *Amgen*.²⁵⁵ The claims in *Amgen* were to all DNA sequences—even those not yet known or described—having a certain function. The claims in the hES cell patents are to all hES cells that stay alive in culture retaining pluri potent activity. In neither case was the matter having this activity defined. Just as many different and unknown types of DNA were covered by the claims in *Amgen*, many different and unknown types of cells are covered by the hES cell product claims. For example, all ES cells are not interchangeable. Scientists have found “[w]ide variations between different [ES cell-]lines, between individual colonies of cells or subclones, and even between individual cells within each colony.”²⁵⁶ Some “researchers have complained of difficulty coaxing [WARF’s] stem cells to grow and differentiate into usable tissue. They press for the creation of many more colonies of stem cells.”²⁵⁷ There were alleged to be only about eighty hES cell-lines in existence on August 9, 2000. hES cells derived from each individual person will contain a unique genome²⁵⁸ certainly making it likely that hES cells with widely varying properties remain to be discovered. Because all varieties of hES cells are not described in the written description, the claims are not enabled or supported by the written description.

The California Supreme Court’s conclusion in *Moore v. Regents of*

254. 66 Fed. Reg. 1099, 1108 n.14 (2001).

255. *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1214 (Fed. Cir. 1991).

256. “These differences in gene activation may or may not trigger abnormalities later in development, and it may only be the cumulative action of many abnormally expressed genes that produces the excessive growth typical in clones.” Ted Agres, *Scientists Clone Solutions to Stem Cell Debate*, 15 SCIENTIST 37 (2001). See D. Humphreys et al., *Epigenetic Instability in ES Cells and Cloned Mice*, 293 SCIENCE 95 (2001).

257. Elias, *supra* note 58.

258. In this context, the WARF patents could be compared to a patent covering all freshly purified DNA. Of course, the PTO would not issue such a patent. Instead, the PTO requires a showing of utility and a strict description of the DNA sequence being claimed. Similar standards should be applied to the hES cell context.

the University of California²⁵⁹ supports the notion that patents for hES cell-lines, but not the hES cell itself, should be upheld. In *Moore*, the court distinguished between freshly dissected cells and human-made cell-lines. A cell-line is different than a freshly dissected cell. A cell-line is an immortalized cell-line that is propagated in carefully controlled culture conditions by scientists.²⁶⁰ Each cell in a cell-line is generally identical, and very likely has different properties from any naturally occurring cell.²⁶¹ Thus, in a very real sense, a cell-line is an "invention" whereas a freshly isolated cell is at most a "discovery," although that is a stretch because most cells are well known.

Once a scientist contributes an inventive alteration to the cell, the cell becomes a unique cell-line: a man-made "invention" that can be described sufficiently narrowly in a patent specification. I propose that a cell only becomes the property of someone after it is transformed into a cell-line. At that point it has distinct characteristics that might be different from other cell-lines, even those derived from the same original cell sample.

This analysis can be extended to the hES cell patent product claims. Although hES cells in general should be unpatentable, patents on specific unique cell-lines developed by the inventors are permissible. Such a policy currently exists with the satisfaction of the enablement requirement by depositing cell-lines in a central depository.²⁶² Indeed, this system has been found adequate for meeting the enablement requirement because of the inherent difficulty in describing cell-lines due to their

259. 793 P.2d 479 (Cal. 1990). The California Supreme Court found that it was permissible for a doctor to use a patient's cells to create a cell-line, and to patent and commercialize that cell-line without compensating the patient.

[T]he patented cell line is both factually and legally distinct from the cells taken from Moore's body. Federal law permits the patenting of organisms that represent the product of "human ingenuity," but not naturally occurring organisms. . . . Human cell lines are patentable because "long-term adaptation and growth of human tissues and cells in culture is difficult—often considered an art . . .," and the probability of success is low. . . . It is this *inventive effort* that patent law rewards, not the discovery of naturally occurring raw materials.

Id. at 492-93. The effect of the holding is thought to be that once a cell leaves a body, it is no longer owned by the person. That is not exactly right: the distinction is between naturally occurring cells and artificially cultured cell-lines. "The distinction between primary cells (cells taken directly from the body) and patented cell lines is not purely a legal one. Cells change while being developed into a cell line and continue to change over time." *Id.* at 493 n.35.

260. See ALBERTS ET AL., *supra* note 24.

261. *Id.*

262. *In re Argoudelis*, 434 F.2d 1390, 1392-93 (C.C.P.A. 1970) (approving the use of deposit to disclose microorganisms); see also 37 C.F.R. §§ 1.801-1.809 (1991). Curiously, the Federal Circuit has found that while the enablement requirement is satisfied by depositing biological material, the written description requirement is not. *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 285 F.3d 1013 (Fed. Cir. 2002).

myriad unknown properties. If describing a single cell-line has been found impossible, then how can description of the entire range of hES cells that may possibly be derived from every existing person be possible? Instead, the same approach should be applied to hES cells: once a unique cell-line is developed, it should be deposited. At this point the enablement requirement will be satisfied and the scientist will have demonstrated a clear inventive step. Moreover, this will promote innovation as scientists continue to seek better cell-lines. If a single patent owner owns all hES cells—both freshly purified hES cells and unique human-made cell-lines—scientists will be less likely to inquire into the development of better hES cell-lines.

4. THE REVERSE DOCTRINE OF EQUIVALENTS

Under the reverse doctrine of equivalents (DOE), a court decides that a defendant has infringed a patent claim, but nevertheless allows that infringement²⁶³ for equitable reasons.²⁶⁴ “The purpose of the ‘reverse’ doctrine is to prevent unwarranted extension of the claims beyond a fair scope of the patentee’s invention.”²⁶⁵ Courts the reverse DOE, rarely use but they may do so when, even though the infringer violates the literal claims, his invention is fundamentally different from or is a radical improvement on the invention covered by the infringed claims. Professor Robert Merges characterizes the reverse DOE as a “safety valve” or a “judicial response to the likelihood of a breakdown in bargaining between inventors who pioneer a new technology and those who later develop key improvements.”²⁶⁶ In this sense, the reverse DOE may be an answer to the tragedy of the anticommons problem.

In *Scripps Clinic & Research Foundation v. Genentech, Inc.*,²⁶⁷ the Federal Circuit remanded to determine whether a method of producing a protein through recombinant DNA techniques should be excused from infringing a patent that claimed the purified natural protein. Genentech’s method was a large economic and scientific advance on Scripps’s method.²⁶⁸ Instead of having to painstakingly purify the protein from human sources, scientists could prepare the protein in bacteria in large amounts, free from human and viral contaminants, relatively quickly and cheaply. Nevertheless, Scripps had claimed the purified pro-

263. See *Boyden Power-Brake Co. v. Westinghouse*, 170 U.S. 537 (1898), for the first appearance of the doctrine.

264. Merges, *supra* note 135, at 91.

265. *Scripps Clinic & Research Found. v. Genentech, Inc.*, 927 F.2d 1565, 1581 (Fed. Cir. 1991).

266. Merges, *supra* note 135, at 75.

267. 927 F.2d 1565.

268. Merges, *supra* note 135, at 93.

tein, and even though Genentech's method for making it was vastly superior, Genentech literally infringed Scripps's claims.

Merges believes that the reverse DOE is justified in *Scripps* on the basis of "the large social welfare loss caused by lack of agreement."²⁶⁹ The value of the improvement was so great as to support the issuance of a property right to the improver. This argument is very similar to the argument made by Judge Learned Hand in *Parke-Davis* in support of patenting a purified product of nature.²⁷⁰ In both cases, the courts seek to reward an important technological advance. In *Parke-Davis* the court found a way to award a patent, whereas in *Scripps* the court found a way to ignore a previous patent. Interestingly, in both cases the patent at issue involved purification of a product of nature. In this sense, in *Scripps* the reverse DOE is an exception to an exception to the rule that inventions must be new.

Another area where the reverse DOE might be appropriately used is in the field of DNA sequences. Uses of the sequences of whole genes might be excused from infringing patent claims to partial sequences of those genes, otherwise known as ESTs.²⁷¹ The basis for excused infringement is that the value of the full sequence would be so great as to characterize its discovery as a "radical improvement" over the pioneer patent claiming the EST sequence.

In light of these two examples, the reverse DOE is highly relevant in the hES cell context. The hES cell patents themselves disclose no obvious therapeutic use for hES cells. In addition, the only commercial use is the sale of the cell-lines to other researchers. Although there are many suggestions for which the cells might be useful, much work and investment is required to realize any therapeutic uses. This is especially true in light of the fact that many envisioned uses will require FDA approval. Any such use will be a big advance on the state of knowledge as presented in the pioneer patent, and as existing in the scientific field at the time of the patent. Any such improvement should be excused from infringing by making use of the reverse DOE doctrine.

Although use of the reverse DOE to excuse future work on hES cells from infringing the WARF patent product claims is desirable, widespread use of this doctrine should be avoided. Patent claims should be respected. Otherwise, a strength of the patent system—the certainty it provides to industry in knowing how to plan its course of research and

269. *Id.* at 94.

270. *Parke-Davis & Co. v. H.K. Mulford Co.*, 189 F. 95 (C.C.S.D.N.Y. 1911); *see also supra* Part III.A.1.b.

271. Michael S. Greenfield, Note, *Recombinant DNA Technology: A Science Struggling with the Patent Law*, 44 STAN. L. REV. 1051, 1078-79 (1992).

development, as well as how to value patent claims in licensing or investment negotiations—will be diminished. Ideally, the PTO should not issue such claims in the first place. The reverse DOE should only be used in extreme cases, such as when the PTO slips up.

B. *Narrow Interpretation of the Scope of Product-of-Nature
Patent Claims*

If broad patent claims covering upstream research are issued by the PTO and are not invalidated by the courts, they should be construed narrowly if possible, since they impede the entrance of competitors and other innovators. In particular, the scope of claims covering purified products of nature such as hES cells should be narrowly construed because they are not only likely upstream discoveries, but in some cases they may not accurately reflect the inventive leap disclosed. The challenge is finding a way to encourage valuable advances in purification or isolation technology without stifling the development of uses for the purified substance. The hope is that the law will optimize the incentives for both pioneer and improvement inventors, so that the market is not dominated by a single firm.²⁷² According to this solution patents may be relatively freely issued, but the scope of the claims should be narrowly tailored by the PTO and narrowly construed by the courts.²⁷³ This solution would be consistent with patents' current value to entrepreneurs as bargaining chips in attracting investment (that is, the PTO would continue to issue patent claims covering such inventions), while not driving away other ventures that may develop similar technologies (that is, the claims issued would only be very narrow).

How should claims' scope be narrowed? Some have suggested that claims' scope be tailored to the innovation's economic value. Thus, their scope would be limited to only what is necessary for the inventor to "reap returns on their inventions sufficient to recover investment in research and development."²⁷⁴ Nevertheless, the PTO does not make economic analyses of industries and the putative effect of the patent application on them, and rightly so; it would be unreasonable to expect patent examiners to attempt to do this. Instead, I propose that patent examiners simply ensure that the claim coverage is coextensive with the

272. Merges & Nelson, *supra* note 155, at 843-44.

273. The PTO is best positioned to ensure that claims do not cover more than the disclosed inventive step. Of course, the courts have a role, especially in the case of the hES cell patents. Alternatively, leaving the solution to the courts introduces uncertainty as to the value of the patent claims. Bargaining costs would likely increase as companies would not be sure what they are receiving by licensing the patent, and patent holders might attempt to seek more than the true value of their claims.

274. Ko, *supra* note 115, at 793.

inventive step and the invention described in the disclosure. For example, with regard to the hES cell patents, the inventive step is both the method of keeping hES cells alive in their pluri potent state in culture without differentiating, and a handful of unique human-made cell-lines. Thus, the scope of the WARF product claims—covering all freshly purified hES cells and cell-lines—is not appropriately defined.

Some of the aforementioned patentability doctrines may be used to define patent scope.²⁷⁵ For example, the enablement and written description requirements could be used to restrict the claims' coverage solely to the hES cell-lines described in the specification or those that are deposited. Unfortunately for WARF, however, it will be difficult for the courts to narrow the scope of the claims in this way. The plain language of the claims indicates that they cover all hES cells. It seems impossible to narrow these claims without reading limitations into them, something the courts are loath to do. Thus, the courts could either invalidate or apply the reverse DOE to the WARF patent product claims. Any significant newly developed use of hES cells should be held to be noninfringing. Such uses would certainly be radical improvements, as the patents do not describe how the cells will be used. While the WARF claims might have to be declared invalid, the PTO should ensure that the scope of future similar patent claims are coextensive with the actual cell-lines described in the specification or deposited in a central bank.

IV. SHOULD HES CELLS BE CATEGORICALLY UNPATENTABLE?

The combination of the WARF patents and President Bush's decision presents a significant barrier to researchers who wish to study and develop therapies using hES cells. Congress could intervene by either removing WARF's property right altogether or requiring compulsory licensing of the patent. Similarly, for future inventions, should the patent system apply different standards to certain types of biological inventions than it does to other inventions? As this article has demonstrated, biological inventions are unique; for example, they often consist of discoveries of products of nature, not necessarily human-made machine-type inventions. Perhaps the patent system should apply a more exacting examination procedure to them. Alternatively, the patent system could categorically refuse to issue patents covering certain materials such as DNA sequences or freshly purified cells or molecules. The next section begins with a discussion of such a generalized categorical ban on

275. It has been suggested that enablement and written description may be the most appropriate patent doctrines for defining scope. *See Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559 (Fed. Cir. 1997); *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200 (Fed. Cir. 1993).

the patentability of certain biotechnology inventions. It is followed by a discussion of whether it would be wise for Congress to create a specific exception to patentability in the case of hES cells, particularly in response to President Bush's political decision.

A. *Should Different Patentability Standards Apply to
Biological Inventions?*

Should biology or certain subsets of biology be treated differently by the patent system? Could the problem of patenting hES cells be dealt with by making such cell purification product claims generally unpatentable?

Presently, patent law does not distinguish between fields as a matter of doctrine.²⁷⁶ This approach has permitted easy justification of patents on living things, computer algorithms, and business methods.²⁷⁷ Yet studies have shown that the importance and role of patents varies greatly between industries.²⁷⁸ Perhaps certain biotechnology inventions should be subject to different patentability considerations than are other inventions.²⁷⁹ Biotechnology discoveries do not fit neatly into the traditional conception of mechanical inventions that supported the development of the patent system.²⁸⁰ Moreover, the question of how to approach the issue of whether products of nature should be patentable never arose in the original context of mechanical inventions.²⁸¹ Keeping in mind patent law's goal of providing incentives for discovery and disclosure of technology, should "Congress revise the patent statutes, revising categories or creating special forms of protection? How do we strike a proper balance between the resulting legal complexity and the simplicity promised by a 'one size fits all' law of patents?"²⁸²

There is already some different treatment of different fields. For

276. The patent system promotes a "one-size-fits-all system, ensuring that the kinds of innovations the law protects are similar enough that a single set of rules is a reasonable approximation of how best to promote progress" Eisenberg, *supra* note 203, at 2084.

277. *Id.*

278. *Id.*; see also Eisenberg, *supra* note 146, at 166-67.

279. But see Frank H. Easterbrook, *Who Decides the Extent of Rights in Intellectual Property?*, in *EXPANDING THE BOUNDARIES OF INTELLECTUAL PROPERTY: INNOVATION POLICY FOR THE KNOWLEDGE SOCIETY* 405, 405 (Rochelle Cooper Dreyfuss et al. eds., 2001). Judge Easterbrook expresses the view that different treatment of different industries is a bad idea because "[w]hen the law of intellectual property is general, most people are apt to support the best possible set of legal rules. . . . Industry-specific rules are the playgrounds of interest groups." *Id.* at 408. "Narrow laws also tend to detract from the force of competition among producers of intellectual property and thus magnify their own shortcomings. More general statutes have been contract-enabling: they create property rights that set the stage for competition and contract." *Id.* at 409.

280. Ko, *supra* note 115, at 777.

281. See *id.*

282. Breyer, *supra* note 213, at 27.

example, the distinction between the predictability of downstream developments resulting from chemical versus mechanical inventions has resulted in a distinct application of the patent system for chemical inventions.²⁸³ Moreover, the Federal Circuit's decision in *Scripps* suggests that the courts might distinguish biotechnology inventions from chemical ones for categorical purposes.²⁸⁴ The *Scripps* court remanded to determine whether, by applying the reverse DOE, a protein made using recombinant DNA methods could escape infringing a claim to the protein purified from its natural source, even though it literally infringed.²⁸⁵ Such an approach had not been previously applied to chemical compounds.²⁸⁶ Another example deals with the enablement requirement. The PTO has allowed this requirement to be satisfied in the area of biotechnology when it is seemingly impossible to adequately describe the invention, by simply depositing an example of the invention, for example, a cell-line. So it is true that patent law doctrines are modified in subtle ways depending on the patent and technology in question; indeed, decisions on which doctrines apply, and how to apply them, are made on a case-by-case basis.

Nonetheless, the courts and the PTO should be wary of cordoning off broad fields—in this case biotechnology or a subset of biotechnology (that is, cells derived from humans)—from other fields. The flexibility of the patent system is a valuable asset as many industries combine to produce inventions. Indeed, some of the most creative and useful inventions arise from the intersecting margins of seemingly distinct industries. For example, bioinformatics—a combination of biotechnology, computer hardware and software and, sometimes, mechanical inventions—has emerged recently as an important subfield of biotechnology. Congress, the courts, and the PTO cannot predict what inventions lie ahead, and thus cannot know the implications of engaging in such a policy. Indeed, in *Chakrabarty*, the Supreme Court expressed its reluctance to declare that life forms were unpatentable for these reasons.²⁸⁷ Although

283. Ko, *supra* note 115, at 794.

Adjustments to mechanical inventions produce predictable consequences. Conversely, a chemical patent's specification teaches little about how varying the chemical's structure or reactive conditions would alter its effects. To explain the less expansive protection they accord chemical arts, courts reason that the breadth of claims a patent's disclosure supports "varies inversely with the degree of unpredictability of the factors involved."

Id. (quoting *In re Fisher*, 427 F.2d 833, 839 (C.C.P.A. 1970)).

284. *Id.* at 788.

285. See *supra* note 267 and accompanying text.

286. See Robert L. Baechtold et al., *Property Rights in Living Matter: Is New Law Required?*, 68 DENV. U. L. REV. 141, 171 (1991).

287. The Supreme Court has said that Congress drafted the patent statutes broadly so they would include as patentable subject matter unforeseeable inventions because "the inventions most

the Court specified that, if any branch were to do so, it should be the legislature, it also hinted about the wisdom of the legislature doing so.²⁸⁸ The Court dismissed the notion that Congress should make a decision prior to invention about allowing patenting because the very nature of invention is that we do not know what innovations are coming next.²⁸⁹ One cannot expect that Congress can anticipate what scientists and engineers will do. The courts and Congress should be very careful about declaring off-limits areas that may need patent protection.

Instead of resorting to new, rigidly defined patentability categories to deal with the patenting of upstream discoveries such as naturally occurring materials like cells and DNA, the PTO should narrowly tailor the claims, as discussed above, to the inventive step described in the specification. Under this approach, product claims to products of nature would rarely be issued unless there is a strong showing of human invention and a compelling, well-developed use. Moreover, the courts should police the PTO by either invalidating or reducing in scope, where possible, overly broad claims to upstream, basic research.

B. *Should Congress Off-Set President Bush's Decision via the Patent System?*

Should Congress intervene in the patent system by making an exception in the case of hES cells, thus relieving some of the pressure applied by President Bush's decision? As part of its deliberations on President Bush's hES cell decision, and on human cloning bills, Congress could specify that WARF's product claims are unenforceable. This would excuse the courts from having to make the decision. A benefit of this approach is that it would be relatively quick; it could be a number of years before a case reaches the courts. Also, companies might not invest in hES cell improvement research for fear of losing a court battle. Congress could intervene either removing the property right altogether or requiring compulsory licensing of the patent.²⁹⁰ If Congress required compulsory licensing then any firm could use the patent, either free-of-charge or for a fee.²⁹¹

Less extreme forms of compulsory licensing can be envisioned;

benefiting mankind are those that 'push back the frontiers of chemistry, physics, and the like.'" *Diamond v. Chakrabarty*, 447 U.S. 303, 316 (1980) (quoting *Great A.&P. Tea Co. v. Supermarket Corp.*, 340 U.S. 147, 154 (1950) (Douglas, J., concurring)).

288. *Id.* ("Congress employed broad general language in drafting § 101 precisely because such invention are often unforeseeable.").

289. *Id.*

290. Congress may subject a patented subject to compulsory licensing as long as it pays reasonable compensation to the patent holder. 28 U.S.C. § 1498(a) (2002).

291. Rai, *supra* note 102, at 816.

afterall, a compulsory license is similar to a contract, and the contract terms could be set by Congress. For example, as a form of compulsory licensing, improving firms might be allowed to use hES cells for experimental uses, but not be permitted to sell them. Eisenberg has argued for an experimental-use exception for research tools.²⁹² Under this approach, use of a patented item in research would be permissible, but once the result of that use is developed into a product, the user would need to negotiate with the patent holder for rights to commercialize. A benefit of this approach is that it concentrates negotiations *ex post* only to those products that will be commercialized. Another benefit is that such final products can be analyzed from a traditional patentability perspective to determine whether they infringe. This approach eliminates the ability of patent holders to stifle research by prohibiting the use of tools that do not appear in the final product.

Yet, it is less certain how effective this approach would be when the research tool appears in the final product. Although hES cells are now used as research tools, final products currently envisioned involve the use of hES cells. Assuming the hES cell claims are not invalidated, there is very little hope that such a final product could escape infringement. Thus, WARF remains in a position of dominant bargaining power, even in an experimental-use-exception regime. Indeed, this is precisely the bargain that WARF is seeking to strike with its contracts that set the terms under which others may use hES cells.²⁹³ What company would carry on a long-term project of developing a final product that includes hES cells with WARF looking over its shoulder?²⁹⁴ In this scenario, in the absence of invalidation of the patent claims, a good solution might be complete compulsory licensing.

In general, however, it is not good policy to use the patent system to ameliorate problems that exist due to other political decisions.²⁹⁵ First, companies thrive on the certainty and predictability associated with patents. In order to foster an environment of successful patent licensing, parties need to be able to value a patent. If it became standard practice to eliminate or diminish patent property rights for political reasons, this would open the door to changes in the value of patents each time a new party took over the Presidency or the Congress. Second, a better way for Congress to deal with the issue is to address President Bush's decision directly. Federal funding of basic hES cell research would be the best way to speed up innovation in the field. Compulsory

292. Eisenberg, *supra* note 101, at 1074-78.

293. See discussion *supra* note 98.

294. See FREDERIC M. SCHERER, INDUSTRIAL MARKET STRUCTURE AND ECONOMIC PERFORMANCE 379, 392 (1970).

295. See Rai, *supra* note 102, at 816.

licensing should only be proposed in extreme cases, such as to ameliorate problems of getting life-saving drugs to developing nations that cannot afford to pay prices as set by developed nations' markets.²⁹⁶ In the absence of such extreme cases, patent law should be removed from politics. Regarding President Bush's decision on hES cells, if Congress can find the votes to overcome WARF's product claims in some way as described above, then perhaps it can instead use those votes to address President Bush's decision directly.

CONCLUSION

This article has discussed some of the theory that must be considered when attempting to determine whether patent claims fail to serve the incentive goals of the patent system. Problems arise because the patent system sometimes focuses too closely on a single invention, ignoring the effects of issuing a property right on the incentives of subsequent inventors. Additionally, problems arise in the specific field of biopharmaceutical inventions because the courts have overlooked the wisdom of enforcing the product-of-nature prohibition on patentability. Based on this theory, this article concludes that the claims issued to WARF covering hES cells are overly broad and detrimental to the field. This problem is exacerbated by President Bush's decision to withhold federal funds for any research performed on hES cells derived from embryos destroyed after August 9, 2001. In light of these obstructions, courts should invalidate or narrowly construe the scope of the WARF product claims. Additionally, Congress may invalidate the WARF hES cell product claims as part of any response to President Bush's hES cell decision. A better approach, though, is to allow standard patent law procedures to take their course. In general, the PTO and the courts should adopt stricter standards by enforcing existing patent law when dealing with the patentability of upstream, basic research, much as it did when dealing with DNA patent applications. In the future, similar situations will surely arise. To avoid the uncertainty presently facing biotechnology companies over how to value such patents, the PTO and courts should consistently strive to issue only claims narrowly tailored to the inventive step as described in the specification.

296. See Section 5(b) of World Trade Organization Ministerial Conference, Fourth Session, *Declaration on the TRIPs Agreement and Public Health*, Doha, Adopted on Nov. 14, 2002; Frederick M. Abbott, *Compulsory Licensing for Public Health Needs: The TRIPS Agenda at the WTO After the Doha Declaration on Public Health*, Occasional Paper 9, Quaker United Nations Office, (Feb. 2002).